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L66 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:275805 HCAPLUS
DN 136:314972
TI Compositions and methods for the transport of biologically active agents across cellular barriers
IN Houston, Lou L.; Sheridan, Philip J.; Hawley, Stephen; Glynn, Jacqueline M.; **Chapin, Steven**; Basu, Amaresh
PA Arizeke Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 378 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K038-00
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 9, 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002028408	A2	20020411	WO 2001-US30832	20011002
	WO 2002028408	A3	20030320		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001096494	A5	20020415	AU 2001-96494	20011002
	EP 1324778	A2	20030709	EP 2001-977368	20011002
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-237929P	P	20001002		
	US 2000-248478P	P	20001113		
	US 2000-248819P	P	20001114		
	US 2001-267601P	P	20010209		

WO 2001-US30832 W 20011002

AB Disclosed herein are complexes and compds. that pass through cellular barriers to deliver compds. into, through and out of cells, and methods of producing and using such complexes and compds. The complexes and compds. of the invention comprise a biol. active portion and a targeting element directed to a **ligand** that confers transcellular, transcytotic or paracellular transporting properties to an agent specifically bound to the **ligand**, with the proviso that the targeting element is not an **antibody**. Also disclosed are complexes and compds. that comprise two or more targeting elements directed to a **ligand** that confers transcellular, transcytotic or paracellular transporting properties to an agent specifically bound to the **ligand**. Preferred **ligands** include but are not limited to the **stalk** of **pIgR**, a **pIgR** domain, an amino acid sequence that is conserved among **pIgR**'s from different animals, and one of several regions of **pIgR** defined herein.

ST drug targeting **pIgR** cell delivery endocytosis

IT Proteins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(AP-1 (adaptor-related protein complex 1), peptides; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adaptor; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Diagnosis
(agents; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Endocytosis
(apical; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Diagnosis
Drug delivery systems
Endocytosis
Human
Macaca fascicularis
Macaca mulatta
Molecular cloning
Peptidomimetics
Pharmacokinetics
Protein sequences
Signal transduction, biological
Test kits
Transformation, genetic
cDNA sequences
(compns. and methods for the transport of biol. active agents across cellular barriers)

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. and methods for the transport of biol. active agents across cellular barriers)

IT Nucleic acids
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. and methods for the transport of biol. active agents across cellular barriers)

IT **Antibodies**
Antigens
Blood-coagulation factors

Carbohydrates, biological studies
Enzymes, biological studies
Growth factors, animal
Hormones, animal, biological studies
Interleukin 2
Interleukin 4
Interleukins
Ligands
Lipids, biological studies
Receptors
Transcription factors
Transport proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for the transport of biol. active agents across cellular barriers)

IT Amniotic fluid
Blood
Lymph
(delivery to; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Body fluid
(interstitial, delivery to; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Biological transport
(intracellular; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Drug delivery systems
(liposomes; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Bladder
Digestive tract
Eye
Lung
Nose
Uterus
Vagina
(lumen; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleic acid-binding; compns. and methods for the transport of biol. active agents across cellular barriers)

IT **Immunoglobulin receptors**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pIgR (polymeric Ig receptor)**;
compns. and methods for the transport of biol. active agents across cellular barriers)

IT Calmodulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(peptides; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(scaffolding; compns. and methods for the transport of biol. active agents across cellular barriers)

IT Drug delivery systems
(targeted; compns. and methods for the transport of biol. active agents across cellular barriers)

IT 407584-44-5 407584-45-6 407584-46-7 407584-47-8 407584-48-9
407584-49-0 407584-50-3 407584-51-4
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(compns. and methods for the transport of biol. active agents across cellular barriers)

IT 7440-05-3, Palladium, biological studies 7440-06-4, Platinum, biological studies 7440-48-4, Cobalt, biological studies 7440-66-6, Zinc, biological studies 9001-92-7, Proteinase 9002-60-2, Corticotropin, biological studies 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9013-05-2, Phosphatase 372092-80-3, Protein kinase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for the transport of biol. active agents across cellular barriers)

IT 245322-12-7 250649-36-6 409334-92-5 409334-93-6 409334-94-7
409334-95-8 409334-97-0 409334-98-1 409334-99-2 409335-01-9
409335-03-1 409335-05-3 409412-43-7 409412-44-8 409412-45-9
409412-46-0 409412-47-1 409412-48-2 409412-49-3 409412-50-6
409412-51-7 409412-52-8 409412-53-9 409412-54-0 409412-55-1
409412-56-2 409412-57-3 409412-58-4 409412-59-5 409412-60-8
409412-61-9 409412-62-0 409412-63-1 409412-64-2 409412-65-3
409412-66-4 409412-67-5 409412-68-6 409412-69-7 409412-70-0
409412-71-1 409412-72-2 409412-73-3 409412-74-4 409412-75-5
409412-76-6 409412-77-7 409412-78-8 409412-79-9 409412-80-2
409412-81-3 409412-82-4 409412-83-5 409412-84-6 409412-85-7
409412-86-8 409412-87-9 409412-88-0 409412-89-1 409412-90-4
409412-91-5 409412-92-6 409412-93-7 409412-94-8 409412-95-9
409412-96-0 409412-97-1 409412-98-2 409412-99-3 409413-00-9
409413-01-0 409413-02-1 409413-03-2 409413-04-3 409413-05-4
409413-06-5 409413-07-6 409413-08-7 409413-09-8 409413-10-1
409413-11-2 409413-12-3 409413-13-4 409413-14-5 409413-15-6
409413-16-7 409413-17-8 409413-18-9 409413-19-0 409413-20-3
409413-21-4 409413-22-5 409413-23-6 409413-24-7 409413-25-8
409413-26-9 409413-27-0 409413-28-1 409413-29-2 409413-30-5
409413-31-6 409413-32-7 409413-33-8
RL: PRP (Properties)
(unclaimed sequence; compns. and methods for the transport of biol. active agents across cellular barriers)

L66 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN **2001:823032** HCAPLUS
DN **137:31596**
TI Immunobiology of **secretory** IgA antibodies
AU Moro, Itaru
CS Department of Dentistry, Nihon University, Japan
SO Nenmaku Men'eki (2001), 113-133, 294. Editor(s): Kiyono, Hiroshi; Ishikawa, Hiromichi; Nagura, Hiroshi. Publisher: Nakayama Shoten, Tokyo, Japan.
CODEN: 69BZKP
DT Conference; General Review
LA Japanese
CC 15-0 (Immunochemistry)
AB A review discussing structures and functions of structural components of **secretory** IgA. The structural components of **secretory** IgA are IgA, J chain, and **secretory** component **polymeric Ig receptor**. The review includes structure and function of **secretory** and membrane IgA; **secretory** IgA expression; structure and function of **secretory** component **polymeric Ig receptor**; genesis of **polymeric Ig receptor**; role of cytokines in **polymeric Ig receptor** expression; and structure and function of J chain.
ST review **secretion** IgA Ig
IT Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(A, **secretory**; **secretory** IgA structural components IgA, J chain, and **secretory** component)

IT Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(A; **secretory** IgA structural components IgA, J chain, and **secretory** component)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**fragments**, J-chain; **secretory** IgA structural components IgA, J chain, and **secretory** component)

IT Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**secretory** component; **secretory** IgA structural components IgA, J chain, and **secretory** component)

L66 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:730836 HCAPLUS
DN 135:287529
TI **Ligands** directed to the non-**secretory** component, non-**stalk** region of **pIgR** and methods of use thereof
IN **Mostov, Keith E.**; **Chapin, Steven J.**; **Richman-Eisenstat, Janice**
PA Regents of the University of California, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM C07K016-28
ICS A61K039-395; A61K048-00; A61K038-00; A61K031-00; A61K031-7088; A61K047-48; C07K019-00; A61P011-00; C07K014-705
CC 15-3 (**Immunochemistry**)
Section cross-reference(s): 1, 3, 8, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001072846	A2	20011004	WO 2001-US9699	20010326 <--
	WO 2001072846	A3	20020404		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002102657	A1	20020801	US 2001-818247	20010326 <--
	EP 1268555	A2	20030102	EP 2001-926437	20010326 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-192197P	P	20000327		
	US 2000-192198P	P	20000327		
	WO 2001-US9699	W	20010326 <--		

AB The invention provides compns. and methods for specific binding to a region of the **polymeric Ig receptor** (**pIgR**) of a cell with the provisos that the **ligand** does not substantially bind to the most abundant form of the **secretory** component (SC) of **pIgR** present in an organ of interest of an animal of interest under physiol. conditions, and does not bind to the **pIgR stalk**. In some embodiments, the **ligand**

decreases cleavage of SC from the **stalk** by at least one-third. The **ligands** and methods of the invention can be used with both birds and mammals. In more preferred embodiments, the animal is a mammal. In the most preferred embodiment, the animal is a human. The **ligand** may be targeted into the cell or may undergo retrograde transcytosis and release at the basolateral side of the cell, and may comprise a biol. active compn.

ST **polymeric Ig receptor secretory** component **ligand; antibody polymeric Ig receptor secretory** component; epithelial cell drug delivery **antibody pIgR**

IT Disulfide group
(**antibody** fragment stabilization; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Cell membrane
(apical, epithelial; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Cell membrane
(basolateral; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Organic compounds, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol.; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT **Antibodies**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fragments; ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Animal
(human; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Drug delivery systems
(immunoconjugates; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Biological transport
(internalization; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Intestine
(large; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)
IT **Animal cell**
Anti-infective agents
Anti-inflammatory agents
Antibiotics
Biliary tract
Bird (Aves)
Cat (Felis catus)
Cattle
Dog (Canis familiaris)
Epithelium
Epitopes
Goat
Horse (Equus caballus)
Lacrimal gland
Liver
Lung
Mammal (Mammalia)
Mammary gland
Molecular cloning
Nose
Organ, animal
Peptidomimetics
Protein sequences
Salivary gland
Sheep
Stomach
Swine
Uterus
Vagina
(**ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)
IT **Antibodies**
Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)
IT Antisense oligonucleotides
CFTR (cystic fibrosis transmembrane conductance regulator)
Carbohydrates, biological studies
Ligands
Lipids, biological studies
Nucleic acids
Proteins, general, biological studies
Radionuclides, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)
IT **Animal cell**
(mammalian; **ligands** or **antibodies** directed to the

non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Drug delivery systems
(mucosal; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT **Immunoglobulin receptors**
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**polymeric Ig**; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Transcytosis
(**receptor**-mediated; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT **Immunoglobulin receptors**
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**secretory** component; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Body, anatomical
(sinus; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT Intestine
Molecules
(small; **ligands** or **antibodies** directed to the non-**secretory** component, non-**stalk** region of **polymeric Ig receptor pIgR** for drug targeting or delivery)

IT 365241-68-5 365241-69-6 365241-70-9 365295-56-3
RL: PRP (Properties)
(unclaimed sequence; **ligands** directed to the non-**secretory** component, non-**stalk** region of **pIgR** and methods of use thereof)

L66 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:756900 HCAPLUS
DN 133:331775
TI Protein transport assays using IR fluorescent labeled **ligands**
IN **Mostov, Keith**; Altschuler, Yoram
PA Regents of the University of California, USA
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM C12Q001-00
ICS C12Q001-02; C12Q001-04; C12Q001-32; G01N033-00; G01N033-53; C07H019-20
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 1, 6, 15
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2000063418	A1	20001026	WO 2000-US10173	20000414 <--

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1999-292274 A 19990415 <--
OS MARPAT 133:331775
AB The invention provides methods and compns. for quant. detecting **ligand** movement across a biol. membrane. The general method comprises the steps of (a) contacting a **ligand** comprising an assay-compatible IR fluorescent label with a receptor under conditions wherein the receptor transports an amt. of the **ligand** across a biol. membrane; and (b) quant. detecting fluorescence as an indicator of the amt. of the **ligand** transported across the membrane. IgA labeled with NN382 or Cy5.5 was used to examine drugs affecting IgA transport in MDCK cells transfected with cDNA for rabbit **pIgR**.
ST protein transport assay IR fluorescent labeled **ligand**; IgA transport drug screening
IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A, detection of drugs affecting transport of, across epithelial cell membranes; protein transport assays using IR fluorescent labeled **ligands**)
IT Fluorescent indicators
Fluorescent probes
(IR fluorescent **ligands**; protein transport assays using IR fluorescent labeled **ligands**)
IT Animal cell line
(MDCK, in detection of drugs affecting transport of IgA across epithelial cell membranes; protein transport assays using IR fluorescent labeled **ligands**)
IT Fluorescent dyes
(as labels; protein transport assays using IR fluorescent labeled **ligands**)
IT Immunoglobulins
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(conjugates, A, with fluorescent labels; protein transport assays using IR fluorescent labeled **ligands**)
IT Transferrins
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(conjugates, with fluorescent labels; protein transport assays using IR fluorescent labeled **ligands**)
IT **Ligands**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(contg. IR fluorescent labels; protein transport assays using IR fluorescent labeled **ligands**)
IT Biological transport
(intracellular; protein transport assays using IR fluorescent labeled **ligands**)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(labeled, contg. IR fluorescent labels; protein transport assays using IR fluorescent labeled **ligands**)
IT Endosome

(membrane; protein transport assays using IR fluorescent labeled **ligands**)

IT Transport proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(norepinephrine-transporting, noradrenaline transport through; protein transport assays using IR fluorescent labeled **ligands**)

IT Transport proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptide-transporting, PEPT1; protein transport assays using IR fluorescent labeled **ligands**)

IT P-glycoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptides and colchicine and vinblastine transport by; protein transport assays using IR fluorescent labeled **ligands**)

IT **Immunoglobulin receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polymeric Ig**, in detection of drugs affecting transport of IgA across epithelial cell membranes; protein transport assays using IR fluorescent labeled **ligands**)

IT Biological transport
Drug screening
Endocytosis
Exocytosis
Fluorescence
Membrane, biological
Microtiter plates
Transcytosis
(protein transport assays using IR fluorescent labeled **ligands**)

IT Receptors
Transferrin receptors
Transferrins
Transport proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein transport assays using IR fluorescent labeled **ligands**)

IT Fluorometry
(scanning; protein transport assays using IR fluorescent labeled **ligands**)

IT Peptides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport of, by P-glycoprotein; protein transport assays using IR fluorescent labeled **ligands**)

IT 29816-01-1D, conjugates with fluorescent labels
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(PEPT1 in pancreatic cells transport of; protein transport assays using IR fluorescent labeled **ligands**)

IT 166547-11-1D, NN382, conjugates with IgA 166799-10-6D, IRD41, conjugates with transferrin 169799-14-8D, Cy7, conjugates with transferrin 172777-84-3D, Cy5.5, conjugates with IgA
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(protein transport assays using IR fluorescent labeled **ligands**)

IT 9004-54-0, Dextran, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein transport assays using IR fluorescent labeled **ligands**)
IT 52-53-9D, Verapamil, conjugates with fluorescent labels 64-86-8D, Colchicine, conjugates with fluorescent labels 865-21-4D, Vinblastine, conjugates with fluorescent labels 186042-32-0D, conjugates with fluorescent labels
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(transport of, by P-glycoprotein; protein transport assays using IR fluorescent labeled **ligands**)
IT 52-53-9, Verapamil 64-86-8, Colchicine 865-21-4, Vinblastine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport of, by P-glycoprotein; protein transport assays using IR fluorescent labeled **ligands**)
IT 51-41-2D, Noradrenaline, conjugates with fluorescent labels
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(transport of, through noradrenaline transporter; protein transport assays using IR fluorescent labeled **ligands**)
IT 51-41-2, Noradrenaline
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport of, through noradrenaline transporter; protein transport assays using IR fluorescent labeled **ligands**)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L66 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN **2000:650656** HCAPLUS
DN **134:206320**
TI Role of J chain in **secretory** immunoglobulin formation
AU Johansen, F.-E.; Braathen, R.; Brandtzaeg, P.
CS Laboratory for Immunohistochemistry and Immunopathology (LIIPAT), Institute of Pathology, University of Oslo, Rikshospitalet, Oslo, N-0027, Norway
SO Scandinavian Journal of Immunology (2000), 52(3), 240-248
CODEN: SJIMAX; ISSN: 0300-9475
PB Blackwell Science Ltd.
DT Journal
LA English
CC 15-3 (Immunochemistry)
AB The joining (J) chain is a small polypeptide, expressed by mucosal and glandular plasma cells, which regulates **polymer** formation of IgA and IgM. J-chain incorporation into **polymeric** IgA (pIgA, mainly dimers) and pentameric IgM endows these antibodies with several salient features. First, a high valency of antigen-binding sites, which makes them suitable for agglutinating bacteria and viruses; little or no complement-activating potential, which allows them to operate in a noninflammatory fashion; and, most importantly, only J-chain-contg. **polymers** show high affinity for the **polymeric Ig receptor** (**pIgR**), also known as transmembrane

secretory component (SC). This epithelial glycoprotein mediates active external transfer of pIgA and pentameric IgM to exocrine **secretions**. Thus, **secretory** IgA (SIgA) and SIgM, as well as free SC, are generated by endoproteolytic cleavage of the **pIgR** extracellular domain. The **secretory** antibodies form the "first line" of defense against pathogens and noxious substances that favor the mucosae as their portal of entry. The J chain is involved in creating the binding site for **pIgR**/SC in the **Ig polymers**, not only by detg. the **polymeric** quaternary structure but apparently also by interacting directly with the **receptor** protein. Therefore, both the J chain and the **pIgR**/SC are key proteins in **secretory** immunity.

ST J chain **secretory** IgA IgM

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A, polymeric; J chain role in **secretory** Ig formation)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A, **secretory**; J chain role in **secretory** Ig formation)

IT B cell (lymphocyte)
(J chain role in **secretory** Ig formation in)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(M, pentameric; J chain role in **secretory** Ig formation)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(M, **secretory**; J chain role in **secretory** Ig formation)

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**fragments**; J chain role in **secretory** Ig formation)

IT Lymphocyte
(plasma cell; J chain role in **secretory** Ig formation in)

IT **Immunoglobulin receptors**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**polymeric Ig**; J chain role in **secretory Ig** formation)

IT Quaternary structure
(protein; J chain role in **secretory** Ig formation)

IT Immunoglobulins
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**secretory** component; J chain role in **secretory** Ig formation)

IT Immunity
(**secretory**; J chain role in **secretory** Ig formation in relation to)

RE.CNT 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L66 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:220716 HCAPLUS
DN 132:261375
TI Immunoglobulin fusion product with immunoglobulin receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention
IN Hiatt, Andrew C.; Ma, Julian K. C.; Lehner, Thomas; **Mostov, Keith E.**
PA USA
SO U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 367,395.
CODEN: USXXAM
DT **Patent**
LA English
IC ICM C12N015-00
ICS C12N015-29; C12N015-82; A01H004-00
NCL 435070100
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 11, 15
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6046037	A	20000404	US 1995-434000	19950504
	CA 2208783	AA	19960711	CA 1995-2208783	19951227
	WO 9621012	A1	19960711	WO 1995-US16889	19951227
	W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SG				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9646088	A1	19960724	AU 1996-46088	19951227
	AU 722668	B2	20000810		
	EP 807173	A1	19971119	EP 1995-944237	19951227
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	CN 1183802	A	19980603	CN 1995-197699	19951227
	US 6303341	B1	20011016	US 1999-312157	19990514
	US 2002159958	A1	20021031	US 2001-982107	20011016
PRAI	US 1994-367395	B2	19941230		
	US 1995-434000	A	19950504		
	WO 1995-US16889	W	19951227		
	US 1999-312157	A1	19990514		

AB Igs of the present invention are useful as therapeutic Igs against mucosal pathogens such as Streptococcus mutans. The Igs contain a protection protein (e.g., the polyimmunoglobulin receptor) that protects the Igs in the mucosal environment. The invention also includes a greatly improved method of producing Igs in plants by producing the protection protein in the same cell as the other components of the Igs. The components of the Ig are assembled at a much improved efficiency. The method of the

invention allows the assembly and high efficiency prodn. of such complex mols. The invention also contemplates the prodn. of Igs contg. protection proteins in a variety of cells, including plant cells, that can be selected for useful addnl. properties. The use of Igs contg. protection proteins as therapeutic **antibodies** against mucosal and other pathogens is also contemplated.

ST Ig fusion receptor protection mucosa caries; dental caries prevention Ig fusion receptor; sequence Ig fusion receptor mucosa protection; plant transgenic manuf Ig fusion receptor

IT Immunoglobulins
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(A; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Immunoglobulins
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(D; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Immunoglobulins
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(E; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Immunoglobulins
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Immunoglobulins
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Guy's 13, fusion products, with Ig receptors; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Ig antigen-binding domain; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Agrobacterium tumefaciens
Alfalfa (Medicago sativa)
Arabidopsis
Dicotyledon (Magnoliopsida)
Immunotherapy
Monocotyledon (Liliopsida)
Mucous membrane
Petunia
Protein sequences
Streptococcus mutans
Streptococcus sobrinus
Tobacco
Tomato
cDNA sequences

(Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Immunoglobulins
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Tooth
(caries, prevention of; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Immunoglobulin receptors
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products, with Igs; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT Transformation, genetic
(transgenic, Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT 144997-23-9DP, Glycoprotein (human **secretory** component protein moiety reduced), fusion products with Ig 170979-93-8DP, fusion products with Ig 180616-69-7DP, Receptor, immunoglobulin (rabbit), fusion products with Ig 180616-70-0DP, Receptor, immunoglobulin (mouse), fusion products with Ig 180686-83-3DP, Receptor, immunoglobulin (rat), fusion products with Ig 180686-85-5DP, fusion products with Ig receptor 180686-87-7DP, fusion products with Ig receptor
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT 140080-71-3DP, fusion products with Ig 140262-61-9DP, fusion products with Ig 153420-82-7DP, fusion products with Ig 153665-28-2DP, fusion products with Ig 159070-18-5DP, fusion products with Ig 180686-84-4DP, fusion products with Ig receptor cDNA 180686-86-6DP, fusion products with Ig receptor cDNA
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

IT 244135-92-0, PN: US5959177 SEQID: 13 unclaimed DNA 244135-94-2, PN: US5959177 SEQID: 14 unclaimed DNA 244135-95-3, PN: US5959177 SEQID: 15 unclaimed DNA 244135-96-4, PN: US5959177 SEQID: 16 unclaimed DNA 244135-97-5, PN: US5959177 SEQID: 17 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; Ig fusion product with Ig receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental caries prevention)

RE.CNT 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(95) Zhou, G; Methods in Enzymology 1983, V101, P433 HCAPLUS

L66 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:1507 HCAPLUS
DN 128:74313
TI Cellular internalization of the **polymeric Ig receptor** and of **antibody ligands** directed to the extracellular **pIgR stalk**
IN **Mostov, Keith E.; Richman-Eisenstat, Janice**
PA Regents of the University of California, USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM C07K016-00
CC 15-3 (**Immunochemistry**)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9746588	A1	19971211	WO 1997-US7944	19970514
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2256304	AA	19971211	CA 1997-2256304	19970514
	AU 9730632	A1	19980105	AU 1997-30632	19970514
	AU 728587	B2	20010111		
	CN 1221428	A	19990630	CN 1997-195238	19970514
	EP 934338	A1	19990811	EP 1997-925515	19970514
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6042833	A	20000328	US 1997-856383	19970514

	JP 2000511432	T2	20000905	JP 1998-500584	19970514
	IL 127238	A1	20010724	IL 1997-127238	19970514
	RU 2191781	C2	20021027	RU 1999-100279	19970514
	US 6340743	B1	20020122	US 1999-475088	19991230
PRAI	US 1996-18958P	P	19960604		
	US 1997-856383	A3	19970514		
	WO 1997-US7944	W	19970514		

AB The present invention is directed to a **ligand** that binds specifically to the **stalk** of a **polymeric Ig receptor** (**pIgR**) of a cell in a **secretory** component-independent manner. Disclosed are methods of attaching and introducing a **ligand** into a cell expressing **pIgR**. The invention provides the means for transporting therapeutic or diagnostic compns. to, into (endocytosis) or across a cell expressing **pIgR**.

ST internalization **polymeric Ig receptor** **ligand**

IT Gene, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CFTR; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** joined to)

IT **Immunoglobulins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Y; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT Diagnosis
Gene therapy
Immunotherapy
Transcytosis
(cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT **Antibodies**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT Anti-infective agents
Anti-inflammatory agents
Antibiotics
Plasmids
(cellular internalization of **polymeric Ig receptor** and of **antibody ligands** joined to)

IT Antisense oligonucleotides
Carbohydrates, biological studies
Lipids, biological studies
Nucleic acids
Proteins, specific or class
Radionuclides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cellular internalization of **polymeric Ig receptor** and of **antibody ligands** joined to)

IT CFTR (cystic fibrosis transmembrane conductance regulator)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cellular internalization of **polymeric Ig receptor** and of **antibody ligands** joined to gene for)

IT Digestive tract
Respiratory tract
(epithelium; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed

to extracellular **pIgR stalk**)

IT **Immunoglobulins**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**fragments**, conjugates, with polylysine; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT **Antibodies**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(humanized; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT **Animal cell**
(mammalian; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT Protein sequences
(of **polymeric Ig receptors** of mammals)

IT **Immunoglobulin receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymeric Ig**; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT Endocytosis
(**receptor**-mediated; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT Biological transport
(retrograde; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT **Antibodies**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(single chain; cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT 25104-18-1D, Poly-L-lysine, **antibody** Fab conjugates
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cellular internalization of **polymeric Ig receptor** and of **antibody ligands** directed to extracellular **pIgR stalk**)

IT 200392-06-9 200392-07-0 200392-08-1 200392-09-2 200513-53-7 200578-06-9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cellular internalization of **polymeric Ig receptor** and of **antibody ligands** targeted to)

L66 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:482531 HCAPLUS
DN 125:191224
TI Regulation of protein traffic in polarized epithelial cells: the **polymeric immunoglobulin receptor** model
AU **Mostov, K. E.**; Altschuler, Y.; **Chapin, S. J.**; Enrich,

C.; Low, S.-H.; Luton, F.; **Richman-Eisenstat, J.**; Singer, K. L.; Tang, K.; Weimbs, T.
CS Department Anatomy, University California, San Francisco, CA, 94143-0452, USA
SO Cold Spring Harbor Symposia on Quantitative Biology (1995), 60(Protein Kinesis: The Dynamics of Protein Trafficking and Stability), 775-781 CODEN: CSHSAZ; ISSN: 0091-7451
PB Cold Spring Harbor Laboratory Press
DT Journal; General Review
LA English
CC 13-0 (Mammalian Biochemistry)
AB A review with 25 refs. The **polymeric Ig receptor** (**pIgR**) provides an excellent model for analyzing the regulation of membrane traffic in polarized epithelial cells. The basolateral sorting signal of the **pIgR** and the pathway and regulation of transcytosis were discussed in detail.
ST review protein transport polarized epithelium; **polymeric Ig receptor** transport epithelium review
IT Proteins, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polymeric Ig receptor** model of regulation of protein traffic in polarized epithelial cells)
IT **Immunoglobulin receptors**
Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**pIgR** (**polymeric Ig receptors**), **polymeric Ig receptor** model of regulation of protein traffic in polarized epithelial cells)
IT Epithelium
(polarized, **polymeric Ig receptor** model of regulation of protein traffic in polarized epithelial cells)
IT Biological transport
(translocation, **polymeric Ig receptor** model of regulation of protein traffic in polarized epithelial cells)

L66 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:54805 HCAPLUS
DN 124:115363
TI Calmodulin binds to the basolateral targeting signal of the **polymeric immunoglobulin receptor**
AU **Chapin, Steven J.**; Enrich, Carlos; Aroeti, Benjamin; Havel, Richard J.; **Mostov, Keith E.**
CS Dep. Anat. Biochem. Biophys., Univ. California, San Francisco, CA, 94143, USA
SO Journal of Biological Chemistry (1996), 271(3), 1336-42 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 15-10 (Immunochemistry)
Section cross-reference(s): 13
AB We have identified a major calmodulin (CaM)-binding protein in rat liver endosomes using 125I-CaM overlays from two-dimensional protein blots. Immunostaining of blots demonstrates that this protein is the **polymeric Ig receptor** (**pIgR**). We further investigated the interaction between **pIgR** and CaM using Madin-Darby canine kidney cells stably expressing cloned wild-type and mutant **pIgR**. We found that detergent-solubilized **pIgR** binds to CaM-agarose in a Ca2+-dependent fashion, and binding is inhibited by the addn. of excess free CaM or the CaM antagonist W-13 (N-(4-aminobutyl)-5-chloro-2-naphthalenesulfonamide), suggesting that

pIgR binding to CaM is specific. Furthermore, **pIgR** is the most prominent 35S-labeled CaM-binding protein in the detergent phase of Triton X-114-solubilized, metabolically labeled **pIgR** -expressing Madin-Darby canine kidney cells. CaM can be chem. cross-linked to both solubilized and membrane-assocd. **pIgR**, suggesting that binding can occur while the **pIgR** is in intact membranes. The CaM binding site is located in the membrane-proximal 17-amino acid segment of the **pIgR** cytoplasmic tail. This region of **pIgR** constitutes an autonomous basolateral targeting signal. However, binding of CaM to various **pIgR** mutants suggests that CaM binding is not necessary for basolateral targeting. We suggest that CaM may be involved in regulation of **pIgR** transcytosis and/or signaling by **pIgR**.

ST calmodulin binding **polymeric Ig receptor**; binding site **polymeric Ig receptor** calmodulin

IT Calmodulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(calmodulin binds to the basolateral targeting signal of the **polymeric Ig receptor**)

IT **Immunoglobulin receptors** **Receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**pIgR** (**polymeric Ig receptors**), calmodulin binds to the basolateral targeting signal of the **polymeric Ig receptor**)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium-dependent binding of calmodulin to the basolateral targeting signal of the **polymeric Ig receptor**)

L66 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN **1994:75120** HCAPLUS
DN **120:75120**
TI Stimulation of transcytosis of the **polymeric immunoglobulin receptor** by dimeric IgA
AU Song, Wenxia; Bomsel, Morgane; Casanova, James; Vaerman, Jean Pierre; **Mostov, Keith**
CS Cardiovasc. Res. Inst., Univ. California, San Francisco, CA, 94143-0452, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**1994**), 91(1), 163-6
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 15-3 (Immunochemistry)
Section cross-reference(s): 6
AB The **polymeric Ig receptor** (**pIgR**) is transcytosed from the basolateral to the apical surface of polarized epithelial cells. The authors have previously shown that phosphorylation of Ser-664 in the cytoplasmic domain of the **pIgR** is a signal for its transcytosis. The authors now report that binding of a physiol. **ligand**, dimeric IgA, to **pIgR** stimulates **pIgR** transcytosis. This stimulation occurs in both the presence or absence of Ser-664 phosphorylation. The authors have used three methods to measure transcytosis of the **pIgR**. The **pIgR** was biosynthetically labeled and its cleavage to **secretory** component after transcytosis was measured. The **pIgR** was labeled with biotin at the basolateral surface. After transcytosis, release of the biotin-labeled **secretory** component into the apical medium was measured. Transcytosis of a **ligand** bound to the **pIgR**

was measured. All three methods indicated that dimeric IgA stimulates transcytosis of the **pIgR**.
ST dimeric IgA transcytosis **polymeric Ig receptor**
IT **Immunoglobulins**
RL: BIOL (Biological study)
(A, dimers, **polymeric Ig receptor**
transcytosis by polarized epithelium stimulation by)
IT Kidney, metabolism
(epithelium, **polymeric Ig receptor**
transcytosis by, dimeric IgA **ligand** stimulation of)
IT **Receptors**
RL: BIOL (Biological study)
(**pIgR** (**polymeric Ig receptors**),
transcytosis of, by polarized epithelium, dimeric IgA **ligand**
stimulation of)
IT Immunoglobulins
RL: BIOL (Biological study)
(**pIgR** receptors, transcytosis of, by polarized epithelium,
dimeric IgA **ligand** stimulation of)
IT Epithelium
(polarized, **polymeric Ig receptor**
transcytosis by, dimeric IgA **ligand** stimulation of)
IT Biological transport
(transcytosis, of **polymeric Ig receptor**,
by polarized epithelium, dimeric IgA **ligand** stimulation of)

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FROM JANUARY 1969 TO DATE.

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L79 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN **1998:386560** BIOSIS
DN **PREV199800386560**
TI Dimerization of the **polymeric immunoglobulin**
receptor controls its transcytotic trafficking.
AU Singer, Karen L.; **Mostov, Keith E. (1)**
CS (1) Dep. Anatomy, Univ. California, San Francisco, CA 94143-0452 USA
SO Molecular Biology of the Cell, (**April, 1998**) Vol. 9, No. 4, pp.
901-915.
ISSN: 1059-1524.
DT Article
LA English
AB Binding of dimeric **immunoglobulin** (Ig)A to the **polymeric**
Ig **receptor** (**pIgR**) stimulates transcytosis of
pIgR across epithelial cells. Through the generation of a series
of **pIgR** chimeric constructs, we have tested the ability of
ligand to promote **receptor** dimerization and the subsequent role
of **receptor** dimerization on its intracellular trafficking. Using
the cytoplasmic domain of the T cell **receptor**-zeta chain as a
sensitive indicator of **receptor** oligomerization, we show that a
pIgR:zeta chimeric **receptor** expressed in Jurkat cells
initiates a zeta-specific signal transduction cascade when exposed to
dimeric or tetrameric IgA, but not when exposed to monomeric IgA. In

addition, we replaced the **pIgR**'s transmembrane domain with that of glycophorin A to force dimerization or with a mutant glycophorin transmembrane domain to prevent dimerization. Forcing dimerization stimulated transcytosis of the chimera, whereas preventing dimerization abolished ligand-stimulated transcytosis. We conclude that binding of dimeric IgA to the **pIgR** induces its dimerization and that this dimerization is necessary and sufficient to stimulate **pIgR** transcytosis.

CC Biochemical Studies - General *10060
Cytology and Cytochemistry - Human *02508
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Membranes (Cell Biology)
IT Chemicals & Biochemicals
dimeric immunoglobulin A; **polymeric immunoglobulin receptor**: dimerization, transcytotic trafficking; T cell receptor zeta chain cytoplasmic domain
IT Miscellaneous Descriptors
ligand-stimulated transcytosis
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Jurkat (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L79 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN **1994:156188** BIOSIS
DN **PREV199497169188**
TI Protein traffic in polarized epithelial cells: The **polymeric immunoglobulin receptor** as a model system.
AU **Mostov, Keith**
CS Dep. Anat., Univ. Calif. San Francisco, San Francisco, CA 94143 USA
SO Journal of Cell Science, (1993) Vol. 0, No. SUPPL. 17, pp. 21-26. ISSN: 0021-9533.
DT General Review
LA English
AB As a model system to study protein traffic in polarized epithelial cells, we have used the **polymeric immunoglobulin receptor**. This **receptor** travels first to the basolateral surface, where it can bind **polymeric** IgA or IgM. The **receptor** is then endocytosed and delivered to endosomes. The **receptor** is sorted into transcytotic vesicles, which are exocytosed at the apical surface. The 103-amino acid cytoplasmic domain of the **receptor** contains several sorting signals. The 17 residues closest to the membrane are an autonomous signal that is necessary and sufficient for basolateral sorting. For rapid endocytosis there are two independent signals, both of which contain critical tyrosine residues. Finally, transcytosis is signaled by phosphorylation of a particular serine.

CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Biophysics - Membrane Phenomena *10508
Movement *12100
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Immunology and Immunochemistry - General; Methods *34502
BC Animalia - Unspecified *33000
IT Major Concepts
Cell Biology; Membranes (Cell Biology); Metabolism; Physiology
IT Miscellaneous Descriptors
IMMUNOGLOBULIN A; IMMUNOGLOBULIN M; PROTEIN SORTING; SORTING SIGNAL;

TRANSCYTOSIS
ORGN Super Taxa
Animalia - Unspecified: Animalia
ORGN Organism Name
animal (Animalia - Unspecified); Animalia (Animalia - Unspecified)
ORGN Organism Superterms
animals

=> d l82 bib ab tot

L82 ANSWER 1 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:164255 BIOSIS
DN PREV200200164255
TI Apical trafficking of wild-type and mutant forms of the **polymeric immunoglobulin receptor.**
AU Low, Seng Hui (1); **Mostov, Keith E.**; Weimbs, Thomas
CS (1) Department of Cell Biology, Lerner Research Institute, Cleveland Clinic Foundation, 9500 Euclid Avenue, NC10, Cleveland, OH, 44195 USA
SO Molecular Biology of the Cell, (**Dec., 2000**) Vol. 11, No. Supplement, pp. 509a. http://www.molbiolcell.org/. print.
Meeting Info.: 40th American Society for Cell Biology Annual Meeting San Francisco, CA, USA December 09-13, 2000
ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 2 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:349921 BIOSIS
DN PREV200000349921
TI The **polymeric immunoglobulin receptor** mediates pneumococcal adherence and invasion across the human nasopharyngeal epithelial cells.
AU Zhang, J. (1); **Mostov, K.**; Lamm, M.; Tuomanen, E. (1)
CS (1) St. Jude Children's Research Hospital, Memphis, TN USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (2000) Vol. 100, pp. 71-72. print.
Meeting Info.: 100th General Meeting of the American Society for Microbiology Los Angeles, California, USA May 21-25, 2000 American Society for Microbiology
. ISSN: 1060-2011.
DT **Conference**
LA English
SL English

L82 ANSWER 3 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:19938 BIOSIS
DN PREV199800019938
TI Role of tyrosine phosphorylation in **ligand**-induced regulation of transcytosis of the **polymeric immunoglobulin receptor.**
AU Luton, Frederic; Cardone, Michael H.; Zhang, Min; **Mostov, Keith E.**
CS Univ. Calif. San Francisco, Dep. Anat., San Francisco, CA 94143-0452 USA
SO Molecular Biology of the Cell, (**Nov., 1997**) Vol. 8, No. SUPPL., pp. 88A.
Meeting Info.: 37th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 13-17, 1997 American Society for Cell Biology
. ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1997:384643 BIOSIS
DN PREV199799683846
TI Evidence of dimerization of the polymeric immuno-globulin receptor upon binding to dIgA.
AU Singer, K. L.; **Mostov, K. E.**
CS Univ. California San Francisco, Dep. Anatomy, San Francisco, CA USA
SO Journal of General Physiology, (1997) Vol. 110, No. 1, pp. 33A.
Meeting Info.: Fifty-First Annual Meeting of the Society of General Physiologists Woods Hole, Massachusetts, USA September 4-6, 1997
ISSN: 0022-1295.
DT **Conference**; Abstract; **Conference**
LA English

L82 ANSWER 5 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:442483 BIOSIS
DN PREV199699164839
TI Regulation of protein traffic in polarized epithelial cells: The **polymeric immunoglobulin receptor** model.
AU **Mostov, K. E. (1)**; Altschuler, Y.; **Chapin, S. J. (1)**; Enrich, C.; Low, S.-H. (1); Luton, F.; **Richman-Eisenstat, J.**; Singer, K. L.; Tang, K.; Weimbs, T.
CS (1) Dep. Anat., Univ. Calif., San Francisco, CA 94143-0452 USA
SO COLD SPRING HARBOR LABORATORY.. Cold Spring Harbor Symposia on Quantitative Biology, (1995) Vol. 60, pp. 775-781. Cold Spring Harbor Symposia on Quantitative Biology; Protein kinesis: The dynamics of protein trafficking and stability.
Publisher: Cold Spring Harbor Laboratory Press 10 Skyline Drive, Plainview, New York 11803, USA.
Meeting Info.: Meeting Cold Spring Harbor, New York, USA 1995
ISSN: 0091-7451. ISBN: 0-87969-070-4 (paper), 0-87969-069-0 (cloth).
DT Book; **Conference**
LA English

L82 ANSWER 6 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:54173 BIOSIS
DN PREV199698626308
TI Dimerization of the **polymeric immunoglobulin receptor** using the transmembrane domain of the glycophorin: Effects of targeting.
AU Singer, K. L.; **Mostov, K. E.**
CS Dep. Anat., Univ. Calif., San Francisco, CA 94143 USA
SO Molecular Biology of the Cell, (1995) Vol. 6, No. SUPPL., pp. 400A.
Meeting Info.: Thirty-fifth Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 9-13, 1995
ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 7 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1995:52893 BIOSIS
DN PREV199598067193
TI Reconstitution of **polymeric immunoglobulin receptor** transcytosis in permeabilized MDCK cells.
AU Apodaca, G.; **Mostov, K. E.**
CS Dep. Anatomy, Univ. Calif., San Francisco, CA 94143 USA
SO Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 379A.
Meeting Info.: Thirty-fourth Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 10-14, 1994
ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 8 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1995:52635 BIOSIS
DN PREV199598066935
TI Interaction of calmodulin with the basolateral targeting signal of the **polymeric immunoglobulin receptor.**
AU **Chapin, S. J. (1)**; Enrich, C.; Aroeti, B. (1); Havel, R. J.; **Mostov, K. E. (1)**
CS (1) Dep. Anat., Univ. Calif., San Francisco, CA 94143 USA
SO Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 334A. Meeting Info.: Thirty-fourth Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 10-14, 1994 ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 9 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1995:52575 BIOSIS
DN PREV199598066875
TI Antisense to G-s inhibits transcytosis of dimeric IgA by the **polymeric immunoglobulin receptor** in Madin-Darby canine kidney cells.
AU Okamoto, C. T.; **Mostov, K. E.**
CS Dep. Anat. Cardiovascular Res. Inst., Univ. Calif., San Francisco, CA 94143-0452 USA
SO Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 323A. Meeting Info.: Thirty-fourth Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 10-14, 1994 ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 10 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1995:51789 BIOSIS
DN PREV199598066089
TI IgA mediates IP3 production and protein kinase C activation in MDCK cells expressing the **polymeric immunoglobulin receptor.**
AU Cardone, M. (1); Smith, B.; Mochly-Rosen, D.; **Mostov, K. (1)**
CS (1) Dep. Anat. Biochem., Univ. California, San Francisco, CA 94143-0452 USA
SO Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 188A. Meeting Info.: Thirty-fourth Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 10-14, 1994 ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 11 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:515737 BIOSIS
DN PREV199497528737
TI The **polymeric immunoglobulin receptor** is the major high affinity calmodulin binding protein in rat liver endosomes.
AU Enrich, C. (1); **Mostov, K. E.**; Havel, J. R.
CS (1) Dep. Biol. Cel. Anat. Patol., Fac. Med., Univ. Barcelona, Barcelona Spain
SO Journal of Hepatology, (1994) Vol. 21, No. SUPPL. 1, pp. S75. Meeting Info.: 29th Annual Meeting of the European Association for the Study of the Liver Athens, Greece September 7-10, 1994 ISSN: 0168-8278.
DT **Conference**
LA English

L82 ANSWER 12 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:379395 BIOSIS

DN PREV199497392395
TI Both the G-s-alpha and beta-gamma subunits of the heterotrimeric G protein, G-S, control the sorting of the **polymeric immunoglobulin receptor** into transcytotic vesicles.
AU Bomsel, Morgane (1); **Mostov, Keith E.**
CS (1) Inst. Cochin de Genetique Moleculaire, 22 rue Mechain, 75014 Paris France
SO Biochemical Society Transactions, (1994) Vol. 22, No. 2, pp. 463-468.
Meeting Info.: 649th Meeting of the Biochemical Society London, England, UK December 19-21, 1993
ISSN: 0300-5127.
DT **Conference**
LA English

L82 ANSWER 13 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:98961 BIOSIS
DN PREV199497111961
TI Internalization of the **polymeric immunoglobulin receptor** is decreased by mutation of a phosphorylated serine in its cytoplasmic domain.
AU Okamoto, C. T. (1); Song, W.; Bomsel, M.; **Mostov, K. E.**
CS (1) Dep. Anat., Univ. Calif., San Francisco, CA 94143-0452 USA
SO Molecular Biology of the Cell, (1993) Vol. 4, No. SUPPL., pp. 437A.
Meeting Info.: Thirty-third Annual Meeting of the American Society for Cell Biology New Orleans, Louisiana, USA December 11-15, 1993
ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 14 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:98265 BIOSIS
DN PREV199497111265
TI Regulation of transcytosis of the **polymeric immunoglobulin receptor** by its physiological **ligand.**
AU Song, W. (1); Bomsel, M.; Casanova, J.; Vaerman, J.-P.; **Mostov, K.**
CS (1) Dep. Anat., Univ. Calif., San Francisco, CA 94143-0452 USA
SO Molecular Biology of the Cell, (1993) Vol. 4, No. SUPPL., pp. 317A.
Meeting Info.: Thirty-third Annual Meeting of the American Society for Cell Biology New Orleans, Louisiana, USA December 11-15, 1993
ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:97639 BIOSIS
DN PREV199497110639
TI Basolateral targeting of the **polymeric immunoglobulin receptor** from the trans-Golgi network and from basolateral endosomes of MDCK cells.
AU Aroeti, B.; Kosen, P. A.; Kuntz, I. D.; Cohen, F. E.; **Mostov, K. E.**
CS Dep. Anatomy, Univ. California, San Francisco, CA 94143 USA
SO Molecular Biology of the Cell, (1993) Vol. 4, No. SUPPL., pp. 208A.
Meeting Info.: Thirty-third Annual Meeting of the American Society for Cell Biology New Orleans, Louisiana, USA December 11-15, 1993
ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 16 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:96951 BIOSIS
DN PREV199497109951

TI Phorbol ester mediated stimulation of transcytosis of the **polymeric immunoglobulin receptor** in MDCK cells involves protein kinase-C alpha translocation.
AU Cardone, M. H. (1); Smith, Bradley L.; Mochly-Rosen, Daria; **Mostov, K. E.**
CS (1) Dep. Anat., Univ. Calif., San Francisco, CA 94143-0452 USA
SO Molecular Biology of the Cell, (1993) Vol. 4, No. SUPPL., pp. 90A.
Meeting Info.: Thirty-third Annual Meeting of the American Society for Cell Biology New Orleans, Louisiana, USA December 11-15, 1993
ISSN: 1059-1524.
DT **Conference**
LA English

L82 ANSWER 17 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1993:263102 BIOSIS
DN PREV199344125252
TI Regulation of transcytosis of the **polymeric immunoglobulin receptor** in MDCK cells by protein kinase C.
AU Cardonne, M. H.; **Mostov, K. E.**
CS Univ. Calif., San Francisco, CA 94143-0452 USA
SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART C, pp. 25.
Meeting Info.: Keystone Symposium on Genetic and In Vitro Analysis of Cell Compartmentalization Taos, New Mexico, USA February 8-14, 1993
ISSN: 0733-1959.
DT **Conference**
LA English

L82 ANSWER 18 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1993:241615 BIOSIS
DN PREV199344114815
TI Membrane traffic and transcytosis in polarized epithelial cells: Signals, mechanisms, and regulation.
AU **Mostov, K. (1)**; Apodaca, G.; Aroeti, B. (1); Song, W. (1); Bomsel, M.
CS (1) Dep. Anat., Univ. Calif., San Francisco, CA 94143-0452 USA
SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART C, pp. 49.
Meeting Info.: Keystone Symposium on Emerging Principles for Vaccine Development: Antigen Processing and Presentations Taos, New Mexico, USA February 8-14, 1993
ISSN: 0733-1959.
DT **Conference**
LA English

L82 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1992:65631 BIOSIS
DN BR42:29531
TI TRANSCYTOSIS OF PLACENTAL ALKALINE PHOSPHATASE **POLYMERIC IMMUNOGLOBULIN RECEPTOR** FUSIONS.
AU APODACA G; **MOSTOV K E**
CS DEP. ANATOMY, UNIVERSITY CALIFORNIA, SAN FRANCISCO, CALIF. 94143.
SO ABSTRACTS OF PAPERS PRESENTED AT THE THIRTY-FIRST ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, BOSTON, MASSACHUSETTS, USA, DECEMBER 8-12, 1991. J CELL BIOL. (1991) 115 (3 PART 2), 195A.
CODEN: JCLBA3. ISSN: 0021-9525.
DT **Conference**
FS BR; OLD
LA English

L82 ANSWER 20 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1990:190357 BIOSIS

DN BR38:90680
TI A SUBDOMAIN OF THE **POLYMERIC IMMUNOGLOBULIN RECEPTOR** CYTOPLASMIC TAIL SPECIFIES BASOLATERAL TARGETING IN MDCK CELLS.
AU CASANOVA J E; **MOSTOV K E**
CS DEP. ANAT., UNIV. CALIF. SAN FRANCISCO, SAN FRANCISCO, CALIF. 94143, USA.
SO SYMPOSIUM ON GENETIC AND IN VITRO ANALYSIS OF CELL COMPARTMENTALIZATION HELD AT THE 19TH ANNUAL MEETINGS OF THE UNIVERSITY OF CALIFORNIA-LOS ANGELES SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, TAOS, NEW MEXICO, USA, FEBRUARY 3-9, 1990. J CELL BIOCHEM SUPPL. (1990) 0 (14 PART C), 38.
CODEN: JCBSD7.
DT **Conference**
FS BR; OLD
LA English

L82 ANSWER 21 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1990:59809 BIOSIS
DN BR38:26229
TI A SUBDOMAIN OF THE **POLYMERIC IMMUNOGLOBULIN RECEPTOR** CYTOPLASMIC TAIL SPECIFIES BASOLATERAL TARGETING IN MDCK CELLS.
AU CASANOVA J E; **MOSTOV K E**
CS DEP. ANATOMY, UC SAN FRANCISCO 94143.
SO TWENTY-NINTH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, HOUSTON, TEXAS, USA, NOVEMBER 5-9, 1989. J CELL BIOL. (1989) 109 (4 PART 2), 295A.
CODEN: JCLBA3. ISSN: 0021-9525.
DT **Conference**
FS BR; OLD
LA English

L82 ANSWER 22 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1989:171974 BIOSIS
DN BR36:83215
TI PHOSPHORYLATION AFFECTS POST-ENDOCYTIC SORTING OF THE **POLYMERIC IMMUNOGLOBULIN RECEPTOR.**
AU CASANOVA J E; **MOSTOV K E**
CS WHITEHEAD INST., CAMBRIDGE, MASS.
SO JOINT MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY AND THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, SAN FRANCISCO, CALIFORNIA, USA, JANUARY 29-FEBRUARY 2, 1989. J CELL BIOL. (1988) 107 (6 PART 3), 447A.
CODEN: JCLBA3. ISSN: 0021-9525.
DT **Conference**
FS BR; OLD
LA English

L82 ANSWER 23 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1989:171930 BIOSIS
DN BR36:83171
TI TRANSCYTOSIS AND SORTING OF THE **POLYMERIC IMMUNOGLOBULIN RECEPTOR.**
AU **MOSTOV K**; CASANOVA J; BREITFELD P
CS WHITEHEAD INST., CAMBRIDGE, MASS.
SO JOINT MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY AND THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, SAN FRANCISCO, CALIFORNIA, USA, JANUARY 29-FEBRUARY 2, 1989. J CELL BIOL. (1988) 107 (6 PART 3), 439A.
CODEN: JCLBA3. ISSN: 0021-9525.
DT **Conference**
FS BR; OLD
LA English

L82 ANSWER 24 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1987:157048 BIOSIS
DN BR32:75175
TI STRUCTURE AND FUNCTION OF THE **RECEPTOR** FOR **POLYMERIC IMMUNOGLOBULINS**.
AU **MOSTOV K E**; FRIEDLANDER M; BLOBEL G
CS WHITEHEAD INST., NINE CAMBRIDGE CENTER, CAMBRIDGE, MA 02142, USA.
SO KAY, J., ET AL. (ED.). BIOCHEMICAL SOCIETY SYMPOSIA, NO. 51. GENES AND PROTEINS IN IMMUNITY; OXFORD, ENGLAND, JULY 1985. XIII+235P. THE BIOCHEMICAL SOCIETY: LONDON, ENGLAND. ILLUS. (1986) 0 (0), 113-116.
CODEN: BSSYAT. ISSN: 0067-8694. ISBN: 0-904498-18-2.
FS BR; OLD
LA English

L82 ANSWER 25 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1987:99426 BIOSIS
DN BR32:49227
TI DELETION OF CYTOPLASMIC TAIL OF THE **POLYMERIC IMMUNOGLOBULIN RECEPTOR** PREVENTS BASOLATERAL LOCALIZATION AND ENDOCYTOSIS.
AU **MOSTOV K**; DE BRUYN KOPS A; DEITCHER D
CS WHITEHEAD INST., CAMBRIDGE, MA.
SO TWENTY-SIXTH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, WASHINGTON, D.C., USA, DEC. 7-11, 1986. J CELL BIOL. (1986) 103 (5 PART 2), 8A.
CODEN: JCLBA3. ISSN: 0021-9525.
DT **Conference**
FS BR; OLD
LA English

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http://www.derwent.com/userguides/dwpi_guide.html <<<

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L103 ANSWER 1 OF 5 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-416628 [44] WPIX
DNC C2002-117522
TI Complex useful for transporting active agent through epithelial barrier, has biologically active portion and target element directed to **ligand** that confers e.g. transcytotic properties to agent specific to **ligand**.
DC B04 D16
IN BASU, A; **CHAPIN, S**; GLYNN, J M; HAWLEY, S; HOUSTON, L L; SHERIDAN, P J
PA (ARIZ-N) ARIZEKE PHARM INC
CYC 98
PI WO 2002028408 A2 20020411 (200244)* EN 379p A61K038-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001096494 A 20020415 (200254) A61K038-00
EP 1324778 A2 20030709 (200345) EN A61K047-48
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002028408 A2 WO 2001-US30832 20011002; AU 2001096494 A AU 2001-96494 20011002; EP 1324778 A2 EP 2001-977368 20011002, WO 2001-US30832 20011002
FDT AU 2001096494 A Based on WO 200228408; EP 1324778 A2 Based on WO 200228408
PRAI US 2001-267601P 20010209; US 2000-237929P 20001002; US 2000-248478P 20001113; US 2000-248819P 20001114
IC ICM A61K038-00; A61K047-48
AB WO 200228408 A UPAB: 20020711
NOVELTY - A complex or compound (I) comprising biologically active portion and a target element (II) directed to a **ligand** (L1) that confers transcellular, transcytotic or paracellular transporting properties to an agent specifically bound to L1, where (II) is not an **antibody**, is new. Alternatively, (I) comprises two or more (II) directed to one or more L1.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a medical device or kit comprising (I);
(2) a diagnostic composition (DC) comprising (I); and
(3) a diagnostic kit comprising DC.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - (I) is useful for delivering a biologically active agent to an animal, for transporting an active agent through an epithelial or mucosal barrier, and for treating or identifying a disease in an animal (claimed).
Dwg.0/26
FS CPI
FA AB; DCN
MC CPI: B04-B01B; B04-C01; B04-D02; B04-E01; B04-G01; B04-H02; B04-H02A; B04-H02D; B04-H19; B04-J01; B04-J03A; B04-L01; B04-N02; B04-N03; B05-A03A; B05-A03B; B11-C07B; B12-K04E; D05-H09
TECH UPTX: 20020711
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Complex: In (I), (II) is a nucleic acid or a polypeptide derived from a calmodulin, an AP-1 golgi adaptor or a bacterial polypeptide, and L1 is polyimmunoglobulin receptor (**pIgR**) stalk or a domain, conserved sequence or their region, or is a polypeptide having an amino acid sequence from LRKED, QLFVNEE, LNQLT, YWCKW, GWYWC, STLVPL, SYRTD and KRSSK, where L1 is in a region selected from R1 (from KRSSK to carboxy terminus of **PIgR**), R2a (from SYRTD to the carboxy terminus of **PIgR**), R2b (from SYRTD to KRSSK), R3a (from STLVPL to the carboxy terminus of **PIgR**), R3b (from STLVPL to KRSSK), R3c (from STLVPL to SYRTD), R4a (from GWYWC to the

carboxy terminus of **PIgR**), R4b (from GWYWC to KRSSK), R4c (from GWYWC to SYRTD), R4d (GWYWC to STLVPL), R5a (from YWCKW to the carboxy terminus of **PIgR**), R5b (from YWCKW to KRSSK), R5c (from YWCKW to SYRTD), R5d (from YWCKW to STLVPL), R5e (from YWCKW to GWYWC), R6a (from LINQLT to the carboxy terminus to **PIgR**), R6b (from LNQLT to KRSSK), R6c (from LNQLT to SYRTD), R6d (from LNQLT to STLVPL), R6e (from LNQLT to GWYWC), R6f (from LNQLT to YWCKW), R7a (from QLFVNEE to the carboxy terminus of **PIgR**), R7b (from QLFVNEE to KRSSK), R7c (from QLFVNEE to SYRTD), R7d (from LNQLT to STLVPL), R7e (from QLFVNEE to GWYWC), R7f (from QLFVNEE to YWCKW), R7g (from QLFVNEE to LNQLT), R8a (from LRKED to the carboxy terminus of **pIgR**), R8b (from LRKED to KRSSK), R8c (from LRKED to SYRTD), R8d (from LRKED to STLVPL), R8e (from LRKED to GWYWC), R8f (from LRKED to YWCKW), R8g (from LRKED to LNQLT) and R8h (from LRKED to QLFVNEE). (I) further comprises a biologically active portion that is not a targeting element. In (I), the compound further comprises a protein transduction domain (PTD) or membrane transport signals (MTS), where biologically active portion is a:
(a) polypeptide including a peptidomimetic, nucleic acid, a lipid, a carbohydrate, a compound or complex comprising a metal which is from platinum(II), palladium(II), zinc and cobalt(III), a small molecule or their functional derivative, where the polypeptide is from growth factor, an interleukin, an immunogen, a hormone, an enzyme, an enzyme inhibitor, an **antibody**, a clotting factor, a receptor, a **ligand** for a receptor, a kinase, a phosphatase, a scaffold protein, an adaptor protein, a dominant negative mutant, a protease, a signaling molecule, a regulatory molecule, transporter, a transcriptional regulator, a nucleic acid binding protein or their functional derivatives, or is from insulin, interleukin (IL)-2, IL-4, human growth hormone (hGH), sCT and hCT;
(b) a nucleic acid; or
(c) second targeting element that is directed to a molecular target other than L1, which is preferably an **antibody** or its derivative,
where the biologically active portion or its metabolite is absorbed from the lumen of an organ into the body of the animal, where lumen is from gastrointestinary, pulmonary, nasal, nasopharyngeal, pharyngeal, buccal, sublingual, vaginal, urogenital, ocular and tympanic lumen, ocular surface, uterine, urethral, bladder, mammary, salivary, lacrimal, respiratory sinus, biliary, sweat gland.
(I) is delivered preferably to the blood, lymph, interstitial fluid or amniotic fluid of the animal or into the body with a pharmocokinetic profile that results in delivery of an effective dose of the compound or its active portion. (I) is capable of undergoing transcellular movement, baseolateral transcytosis, apical endocytosis, basolateral exocytosis, intracellular transport, and the complex or compound or its active portion is delivered to an intracellular compartment and is transported across the cellular barrier. In (I) comprising two or more (II), one of the (II) is identical or substantially identical, or different to one another (II). Preferably, (I) comprises n number of (II), where one or more of desirable attributes of the compound is enhanced as compared to a second compound having m targeting elements, where n and m are both whole integers, and n greater than m, where one or more desirable attributes is a change in affinity or avidity for L1, where a pharmacological property is from half-life, decreased **secretion**, efficacy and selectivity. (I) further comprises a detectable moiety.
Preferred Composition: PC further comprises antiproteases or carrier polypeptides.

ABEX UPTX: 20020711

ADMINISTRATION - (I) is administered through oral, rectal (e.g. an enema or suppository) aerosol (e.g. for nasal or pulmonary delivery), parenteral or topical routes. Dosage of (I) 0.01-100, preferably 0.01-0.1 micro-g/kg.
EXAMPLE - Single chain Fv **antibody** fragments (sFv) directed to epitopes in defined regions in polyimmunoglobulin receptor (**pIgR**) amino acid sequence was used in vitro genetic manipulation has been used to alter the reading frame of sFv5A to create derivatives that have

substitutions or insertions of amino acids with reactive sites. The template, pSyn expression vector encoding sFv5A, was amplified using primers 5'-AAATACCTATTGCCTACGGCAGCC-3' and 5'-CGGAATTCCTACTAGCAGCCACCGCCACCTGCGGCCGCTAGGACGGTGACCTTGGTCCC-3'. The polymerase chain reaction (PCR) product was cleaved with BamHI and EcoRI and ligated into expression vector DNA, where the resultant expression construct encoded sFv5A-G4Cys which had, from an amino-to carboxy-terminal direction, a pelb leader sequence (for **secretion** in Escherichia coli encoded by vector sequences, sFv5A-Cys i.e. a heavy chain variable region, a spacer sequences (GGGGS repeated three times i.e. (G4S)3), a heavy chain variable region, another G4S linker, and a C-terminal cysteine residue that had been introduced into the sFv relative to sFv5A. Chemical conjugates of salmon calcitonin and sFv5AG4-Cys were prepared. Transcytosis assays were performed with sFv5A-G4Cys and with sFv5A-G4Cys-calcitonin conjugates. The transcytosis assays with sFv5A-G4Cys showed that the sFv5A-G4Cys preparation was a mixture of monomers and dimers. A portion of the sFv preparation migrates as a dimer on non-reducing sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). The dimer species was probably produced by covalent or non-covalent interactions that occurred prior to boiling in SDS. Thus, by comparing the monomer and dimer bands on the gel, one can monitor monomer and dimer transcytosis in the same sample. Transcytosis of sFv5A-G4Cys dimers was typically greater than 10 %, whereas transcytosis sFv5A-G4Cys monomers was usually less than 10 often less than 5 %. The transcytosis assays with sFv5A-G4Cys showed that the preparation of monomer Fv5A-G4Cys-calcitonin that was tested shows 2 conjugate species on SDS-PAGE. These species of conjugates behave differently. Transcytosis of the gel-monomer conjugate was relatively inefficient, resembling that of the sFv5A-G4Cys monomer. In contrast, transcytosis of the gel-dimer conjugate was relatively efficient.

L103 ANSWER 2 OF 5 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
AN **2001-611619** [70] WPIX
DNC **C2001-182806**
TI New **ligands** binding to a specific region of a **polymeric immunoglobulin receptor**, useful for transporting therapeutic or diagnostic compositions into or across cells expressing **pIgR** e.g. in drug delivery.
DC B04 D16
IN **CHAPIN, S J; MOSTOV, K E; RICHMAN-EISENSTAT, J**
PA (REGC) UNIV CALIFORNIA; (CHAP-I) CHAPIN S J; (MOST-I) MOSTOV K E; (RICH-I) RICHMAN-EISENSTAT J
CYC 96
PI WO 2001072846 A2 20011004 (200170)* EN 102p C07K016-28 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001052970 A 20011008 (200208) C07K016-28 <--
US 2002102657 A1 20020801 (200253) C12P021-04
EP 1268555 A2 20030102 (200310) EN C07K016-28 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001072846 A2 WO 2001-US9699 20010326; AU 2001052970 A AU 2001-52970 20010326; US 2002102657 A1 Provisional US 2000-192197P 20000327, Provisional US 2000-192198P 20000327, US 2001-818247 20010326; EP 1268555 A2 EP 2001-926437 20010326, WO 2001-US9699 20010326
FDT AU 2001052970 A Based on WO 200172846; EP 1268555 A2 Based on WO 200172846
PRAI US 2000-192198P 20000327; US 2000-192197P 20000327; US 2001-818247 20010326
IC ICM **C07K016-28**; C12P021-04

ICS A61K031-00; A61K031-7088; A61K038-00; **A61K039-395**; A61K047-48; A61K048-00; A61P011-00; C07K019-00; C12N005-06
ICA **C07K014-705**
AB WO 200172846 A UPAB: 20011129
NOVELTY - **Ligands** that bind specifically to a region of an animal cell **polymeric immunoglobulin receptor** (**pIgR**) are new. The **pIgR** cleaves to produce a stalk region remaining attached to the cell and a **secretory** component existing in the organ of interest in several forms. The **ligands** do not bind to the stalk or the most abundant form of SC present in the organ under physiological conditions.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a **ligand** as above in which the **ligand** does not substantially bind to a peptide comprising 31 amino acids that are cell-membrane-proximal to the initial cleavage site;

(2) a **ligand** as above in which **ligand** binding reduces proteolytic cleavage of SC by at least one-third compared to SC cleavage from cells without **ligand** binding;

(3) introducing the novel **ligand** or the **ligand** of (1) or (2) into a cell (optionally an epithelial cell) of an animal organ, by binding **ligand** to **pIgR**;

(4) a conjugate fusion protein or complex comprising a **ligand** as in (2) and a biologically active component;

(5) attaching a **ligand** of (2), or conjugate fusion protein or complex of (4), to a cell expressing **pIgR**, by binding **ligand** to receptor, optionally in which **ligand** is internalized into the cell after binding; and

(6) transcytosing a **ligand** from an apical to a basolateral side of a cell expressing **pIgR** of an animal organ, by binding the novel **ligand** or the **ligand** of (1) or (2) to **pIgR**.

USE - The **ligands** are useful for transporting therapeutic or diagnostic compositions into or across cells expressing **pIgR**, useful to introduce or transport **ligands** such as **antibodies** and/or to deliver biologically active components such as proteins, nucleic acids or detectable labels. They are used to deliver therapeutic compositions to mucosal surfaces such as the gastro-intestinal tract, respiratory system etc. in humans. They are also useful to label cells expressing **pIgR**, e.g. to distinguish epithelial cells from a mixed cell population in pathology studies or to aid in carcinoma diagnosis (since **pIgR** expression is reduced in carcinomas relative to normal epithelium). They can also be used to deliver veterinary compositions, especially in mammals such as farm, domestic or wild mammals or birds e.g. birds reared for human consumption.

Dwg.0/5
FS CPI
FA AB; DCN
MC CPI: B04-C01B; B04-C01C; B04-G01; B04-N04; B11-C07A; B12-K04A; D05-H09; D05-H11
TECH UPTX: 20011129
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Ligands**: The **ligand** is an **antibody**, particularly a humanized **antibody**, and the animal is a bird or a mammal, especially a human. The organ of interest is preferably a lung, small intestine, large intestine, liver-biliary tree, stomach, salivary gland, vagina, lacrimal gland, uterus, mammary gland, nasal passage, or sinus. The **ligand** may optionally further comprise a biologically active component (e.g. a polynucleotide, protein, radioisotope, lipid, carbohydrate, peptidomimetric, antiinfective, antibiotic, or small molecule), especially when the organ is a lung and the component is a polynucleotide encoding the wildtype cystic fibrosis transmembrane conductance regulator. Preferred Methods: Introducing a **ligand** into a cell of (3) uses

a **ligand** of (2). The rate of internalization of a first **ligand** binding to SC can be increased in cells **secreting pIgR** from an apical surface by binding **pIgR** to **ligand** of (2), and binding first **ligand** to the SC. The rate of transcytosis a first **ligand** binding to SC from an apical to a basolateral side of a cell can be increased in animal cells **secreting pIgR** by binding **pIgR** at the cell apical side to **ligand** of (2), and binding first **ligand** to the SC.

ABEX UPTX: 20011129

SPECIFIC SEQUENCES - **Ligands** binding to epitope sequences (I)-(VII) are specifically claimed. Also claimed are **ligands** binding to one of 30 26-131 residue peptides derived from human **pIgR** (all fully defined in the specification). GlnAspProArgLeuPhe (I) LeuAspProPheLeuPhe (II) LysAlaIleGlnAspProArgLeuPhe (III); LeuAspProArgLeuPheAlaAspGluArgIle (IV); AspGluAsnLysAlaAsnLeuAspProArgLeuPhe (V) ArgLeuPheAlaAspGluArgGluIle (VI); LeuAspProArgLeuPheAlaAspGlu (VII).

EXAMPLE - A Fab fragment reactive to the B region of human **pIgR** was produced routinely and linked to poly (L-lysine) as previously described (Ferkol et al., J. Clin. Invest., 92:2394-2400 (1993)). A plasmid containing the wildtype cystic fibrosis transconductance regulator (CFTR) gene was ligated to a cytomegalovirus early promoter and inserted into pCB6. Plasmid DNA was combined with Fab-polylysine in 3M NaCl to produce Fab-polylysine-DNA complex. Complex was dissolved in 0.1 ml phosphate buffered saline and 100 micro-l applied into nares of anesthetized, pathogen-free Sprague-Dawley rats to target the CFTR gene into cells expressing **pIgR**. CFTR transcription was assayed by immunofluorescence assay of CFTR protein; no results are given.

L103 ANSWER 3 OF 5 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-665249 [64] WPIX
DNN N2000-493019 DNC C2000-201579
TI Quantitatively detecting **ligand** movement across a biological membrane, comprises contacting assay-compatible infrared fluorescent labeled **ligands** with a receptor.
DC B04 D16 E23 E24 S03
IN ALTSCHULER, Y; **MOSTOV, K**
PA (REGC) UNIV CALIFORNIA
CYC 21
PI WO 2000063418 A1 20001026 (200064)* EN 23p C12Q001-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 2000042455 A 20001102 (200107) C12Q001-00
ADT WO 2000063418 A1 WO 2000-US10173 20000414; AU 2000042455 A AU 2000-42455 20000414
FDT AU 2000042455 A Based on WO 200063418
PRAI US 1999-292274 19990415
IC ICM C12Q001-00
ICS C07H019-20; C12Q001-02; C12Q001-04; C12Q001-32; G01N033-00; G01N033-53
AB WO 200063418 A UPAB: 20001209
NOVELTY - Quantitatively detecting **ligand** movement across a biological membrane, comprising contacting a **ligand** comprising an assay-compatible infrared fluorescent label with a receptor, where the receptor binds and transports the **ligand** across a biological membrane, and quantitatively detecting fluorescence to indicate **ligand** transport, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for identifying an agent which modulates movement of a **ligand** across a membrane, comprising:

(a) contacting a **ligand** comprising a compatible fluorescent

label with a receptor, in the presence of a candidate agent, under conditions where in the absence of the agent the receptor transports a first amount of the **ligand** across a membrane;

(b) quantitatively detecting fluorescence as an indicator of a second amount of the **ligand** transported across the membrane; and

(c) comparing the two amounts of transported **ligand**, a difference indicates that the agent modulates movement of the **ligand** across the membrane.

USE - For detecting the movement of macromolecules across biological membranes, and for identifying modulators of the molecular transport (claimed). The macromolecules may be e.g. hormones, cytokines, antibiotics, cytotoxins, chemokines, chemotactic factors, growth factors or neurotransmitters.

ADVANTAGE - The novel method uses infrared labels which are sensitive enough to replace the most sensitive existing labels, such as radiolabels and fluorescent labels, and do not interfere with the transport process. Radiolabels are unsuitable for high-throughput application, and fluorescent label use is limited by spectroscopic interference, the infrared labels overcome these problems.

Dwg.0/0

FS CPI EPI

FA AB; GI; DCN

MC CPI: B04-H01; B04-J01; B06-D01; B06-D13; B06-D18; B08-D01; B11-C07B3; B12-K04; D05-H09; E23; E24-A03

EPI: S03-E14H4

TECH UPTX: 20001209

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The membrane comprises a plasma or endosomal membrane and the transport across the membrane is by endocytosis, exocytosis or translocation. The membrane may alternatively comprise a layer of cells and the transport across the membrane is by transcytosis. The **ligand** is a protein, e.g. immunoglobulin (Ig)A or transferrin, and the detecting step uses a scanning fluorimeter. The method is repeated in massive parallel in distinct elements of an assay array, preferably distinct wells of a multiwell plate. The label comprises a dye having formula (I).

R1, R6, R7 and R12 = independently, substituted or unsubstituted V elements, substituted or unsubstituted VI elements, or substituted or unsubstituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalkyl, heteroaryl, and acyl substituents;

R2-R5 and R8-R11 = independently, substituted or unsubstituted alkyl, alkenyl, alkynyl, aryl, heteroalkyl, heteroaryl, and acyl substituents; and

R13 = substituted or unsubstituted aryloxy or heteroaryloxy.

ABEX UPTX: 20001209

EXAMPLE - Madin-Darby canine kidney epithelial cells were cultured transfected in permeable filter supports to form a well polarized monolayer, essentially reconstituting a simple epithelial tissue, with an apical surface in contact with the overlying medium. Material added to the medium underneath the filter can diffuse through the filter to reach the basolateral surface. For immunoglobulin (Ig)A transport, the cells were transfected with cDNA for rabbit **pIgR**, and the exogenously expressed **pIgR** functions as in vivo. IgA is labeled and added to the basolateral medium. Endocytosis was allowed to proceed for 10 minutes at 37 degrees C, and the cells were washed extensively during a 5 minute period. Finally, the release of IgA into the apical medium, or onto the basolateral medium was followed by sampling the medium over a 2 hour period. Detection of transcytosed IgA labeled with several infrared dyes was easily accomplished, by using 0.3 micro-g infrared fluorescent IgA. Only 0.27 % of the total apical medium was spotted on the filter, but the very small amount of transcytosed IgA was detected on the apical side of the cells. The system was found to be 170-280 fold more sensitive than radio-iodination

L103 ANSWER 4 OF 5 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
AN **2000-549134** [50] WPIX
DNC **C2000-163952**
TI Novel polypeptides containing **pIgR**-binding domains used for targeting and transport to the mucosal epithelia, in the treatment of disorders accessible to the mucosal epithelia, e.g. asthma.
DC B04 D16
IN CAPRA, J D; HEXHAM, J M; MANDECKI, W; WHITE, K
PA (DGIB-N) DGI BIOTECHNOLOGIES; (OKLA-N) OKLAHOMA MEDICAL RES FOUND; (TEXA) UNIV TEXAS SYSTEM; (DGIB-N) DGI BIOTECHNOLOGIES INC
CYC 91
PI WO 2000047611 A2 20000817 (200050)* EN 137p C07K014-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000027597 A 20000829 (200062) C07K014-00
EP 1151000 A2 20011107 (200168) EN C07K014-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002539771 W 20021126 (200307) 166p C12N015-09
ADT WO 2000047611 A2 WO 2000-US3650 20000211; AU 2000027597 A AU 2000-27597 20000211; EP 1151000 A2 EP 2000-906030 20000211, WO 2000-US3650 20000211; JP 2002539771 W JP 2000-598527 20000211, WO 2000-US3650 20000211
FDT AU 2000027597 A Based on WO 200047611; EP 1151000 A2 Based on WO 200047611; JP 2002539771 W Based on WO 200047611
PRAI US 1999-119932P 19990212
IC ICM C07K014-00; C12N015-09
ICS A61K038-00; A61K045-00; A61K047-48; A61P001-00; A61P001-12; A61P001-14; A61P001-16; A61P001-18; A61P011-00; A61P011-06; A61P013-12; A61P029-00; A61P031-00; A61P031-04; A61P031-10; A61P031-14; A61P031-16; A61P031-18; A61P031-20; A61P031-22; A61P033-02; A61P035-00; C07K014-47; **C07K014-705**; C07K019-00; C12N015-10; C12N015-62
AB WO 200047611 A UPAB: 20001010
NOVELTY - A 10-50 residue peptide (I) comprising a **pIgR**-binding domain, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a fusion protein comprising a **pIgR**-binding domain covalently linked to a non-**antibody** peptide or polypeptide;
(2) a polynucleotide encoding the fusion protein of (1);
(3) targeting an agent to a mucosal epithelium comprising administering to a mammal a targeting complex comprising the agent and (I), the complex binds to, and is taken up by, cells expressing **pIgR**, and is transported to the mucosal epithelium;
(4) targeting a non-**antibody** peptide or polypeptide to a mucosal epithelium, comprising administering the fusion protein of (1) to a mammal, the protein binds to, and is taken up by, cell expressing **pIgR**, and is transported to the mucosal epithelium;
(5) delivering an agent to a cell, comprising contacting (I) with a cell expressing **pIgR**; and
(6) delivering a non-**antibody** peptide or polypeptide to a cell, comprising contacting the fusion protein of (1) with a cell expressing **pIgR**.
ACTIVITY - Antiasthmatic; antiinflammatory; antiinfectious; cytostatic; antiulcer; antidiarrheal; hepatropic; virucide; vasotropic; anti-human immunodeficiency virus; antibacterial. No biological data is given.
MECHANISM OF ACTION - None given.
USE - For targeting and transport to the mucosal epithelium

(claimed), for the prevention or treatment of diseases, ailments or conditions that are accessible to mucosal epithelia, including asthma, bronchitis, emphysema, cystic fibrosis, bronchiectasis, bronchiolitis, pulmonary edema, viral tracheobronchitis, sleep apnea syndrome, infectious diseases, neoplastic conditions, Loffler's syndrome, kyphocliosis, dysphagia, peptic ulcers, diarrheal diseases, ulcerative colitis, Crohn's disease, hepatitis, cirrhosis, hemorrhoids, systemic vasculitis, acquired immunodeficiency syndrome, gonorrhea, syphilis and chlamydia. (I) can be attached to a detectable label for use in diagnostics.
Dwg.0/8

FS CPI
FA AB; DCN
MC CPI: B04-C01; B04-E02; B04-E03; B04-N04; B04-N04A; B12-K04A; B14-A01; B14-E02; B14-E04; B14-E08; B14-E10C; B14-F02; B14-G01B; B14-H01; B14-K01; B14-N07C; B14-N12; D05-C11; D05-H09; D05-H12C; D05-H17C
TECH UPTX: 20001010
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Peptide: (I) is 10, 15, 20, 25, 30, 35, 40, 45 or 50 residues in length, and further comprises a linking moiety, preferably SMTP, SPDP, LC-SPDP, Sulfo-LC-SDPD, SMCC, Sulfo-SMCC, MBS, Sulfo-MBS, SIAB, Sulfo-SIAB, SMPM, Sulfo-SMPB, EDC/Sulfo-NHS, or ABH, attached to the peptide. The linking moiety may be further attached to an agent, preferably a peptide, polypeptide, oligonucleotide, polynucleotide, detachable label or drug. The polypeptide is an enzyme, **antibody** region, region mediating protein-protein interaction, cytokine, growth factor, hormone, toxin, tumor suppressor, transcription factor, or apoptosis inducer. The polynucleotide encodes a polypeptide, a single chain **antibody**, an antisense construct or a ribozyme. The detectable label is rhodamine, fluorescein, green fluorescent protein or a radiolabel. The drug is an antibiotic, DNA damaging agent, enzyme inhibitor, or metabolite. Alternatively, (I) further comprises a non-**pIgR** targeting agent linked to the peptide. The targeting agent is an antigen binding domain of an **antibody**, a receptor **ligand** or **ligand** binding domain. (I) may comprise two **pIgR**-binding domains, and further comprise the linking agent and the agent.
Preferred Fusion Protein: The domain is Calpha3 domain. The non-**antibody** peptide or polypeptide is an enzyme, **antibody** region, region mediating protein-protein interaction, cytokine, growth factor, hormone, toxin, tumor suppressor, transcription factor, or apoptosis inducer.
Preferred Complex: The targeting complex further comprises a non-**pIgR** targeting agent.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Prior to performing the method of (5), the cell is transformed with an expression construct encoding **pIgR** under the control of a promoter.
Preparation: (I) can be produced by standard recombinant techniques.
ABEX UPTX: 20001010
SPECIFIC POLYPEPTIDES - (I) comprises one of 41 polypeptide sequences containing 9-45 residues, all fully defined in the specification, e.g. GlnGluProSerGlnGlyThrThrThr, ArgGlyGlyAsnGlyAlaLeuSerTrpArgGlyPheGlyTrpAla HisAspSerTrpPheProTrpPheGlyGly, and GlyTrpLeuGlyGluGlyTrpTrpGluLeuLeu (claimed).

ADMINISTRATION - The mucosal epithelium targeting complex is administered by oral, inhalation, ocular, nasal, vaginal, rectal, intravenous, subcutaneous, intramuscular, or intraarterial routes.

EXAMPLE - No relevant examples are given.

L103 ANSWER 5 OF 5 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN
AN **1998-042123** [04] WPIX
DNC **C1998-014108**

TI **Ligand** that binds the stalk of a cell's **polymeric immunoglobulin receptor** - useful to target to, into or across mammalian epithelial cell biologically active component, e.g. nucleic acid, protein, lipid, carbohydrate, etc.

DC B04

IN **MOSTOV, K E; RICHMAN-EISENSTAT, J; MOSTOV, K**

PA (REGC) UNIV CALIFORNIA

CYC 77

PI WO 9746588 A1 19971211 (199804)* EN 42p C07K016-00
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN YU
AU 9730632 A 19980105 (199821) C07K016-00
EP 934338 A1 19990811 (199936) EN C07K016-00
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1221428 A 19990630 (199944) C07K016-00
US 6042833 A 20000328 (200023) A61K038-16
JP 2000511432 W 20000905 (200047) 46p C12N015-09
AU 728587 B 20010111 (200108) C07K016-00
IL 127238 A 20010724 (200147) C07K016-00
US 6340743 B1 20020122 (200208) C07K016-28 <--
RU 2191781 C2 20021027 (200281) C07K016-42

ADT WO 9746588 A1 WO 1997-US7944 19970514; AU 9730632 A AU 1997-30632 19970514; EP 934338 A1 EP 1997-925515 19970514, WO 1997-US7944 19970514; CN 1221428 A CN 1997-195238 19970514; US 6042833 A Provisional US 1996-18958P 19960604, US 1997-856383 19970514; JP 2000511432 W WO 1997-US7944 19970514, JP 1998-500584 19970514; AU 728587 B AU 1997-30632 19970514; IL 127238 A IL 1997-127238 19970514; US 6340743 B1 Provisional US 1996-18958P 19960604, Div ex US 1997-856383 19970514, US 1999-475088 19991230; RU 2191781 C2 WO 1997-US7944 19970514, RU 1999-100279 19970514

FDT AU 9730632 A Based on WO 9746588; EP 934338 A1 Based on WO 9746588; JP 2000511432 W Based on WO 9746588; AU 728587 B Previous Publ. AU 9730632, Based on WO 9746588; US 6340743 B1 Div ex US 6042833; RU 2191781 C2 Based on WO 9746588

PRAI US 1996-18958P 19960604; US 1997-856383 19970514; US 1999-475088 19991230

IC ICM A61K038-16; C07K016-00; **C07K016-28**; C07K016-42; C12N015-09
ICS A61K039-385; **A61K039-395**; C07K016-46; C12N015-13

AB WO 9746588 A UPAB: 19980126
Ligand that specifically binds the stalk of a **polymeric immunoglobulin receptor** (**pIgR**) of a cell, but not the **secretory** component of **pIgR** under physiological conditions, is claimed.
USE - The **ligand**, which can be introduced into a cell expressing a **pIgR** by attaching to the stalk of the **pIgR** , can be used to target to, into or across the apical or basolateral surface of a mammalian epithelial cell, a biologically active component selected from a nucleic acid (preferably encoding the wild type cystic fibrosis transmembrane conductance regulator), protein, radioisotope, lipid or carbohydrate, e.g. an anti-inflammatory, antisense oligonucleotide, antibiotic or anti-infective.
Dwg.0/0

FS CPI

FA AB

MC CPI: B04-G21; B04-G22; B04-N02A; B11-C07A; B12-K04

=> fil dpci
FILE 'DPCI' ENTERED AT 07:41:21 ON 23 JUL 2003

FILE LAST UPDATED: 21 JUL 2003 <20030721/UP>
PATENTS CITATION INDEX, COVERS 1973 TO DATE

>>> LEARNING FILE LDPCI AVAILABLE <<<

=> d all tot l113

L113 ANSWER 1 OF 3 DPCI COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-611619 [70] DPCI
DNC C2001-182806
TI New ligands binding to a specific region of a polymeric immunoglobulin receptor, useful for transporting therapeutic or diagnostic compositions into or across cells expressing pIgR e.g. in drug delivery.
DC B04 D16
IN **CHAPIN, S J; MOSTOV, K E; RICHMAN-EISENSTAT, J**
PA (REGC) UNIV CALIFORNIA; (CHAP-I) CHAPIN S J; (MOST-I) MOSTOV K E; (RICH-I) RICHMAN-EISENSTAT J
CYC 96
PI WO 2001072846 A2 20011004 (200170)* EN 102p C07K016-28 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001052970 A 20011008 (200208) C07K016-28 <--
US 2002102657 A1 20020801 (200253) C12P021-04 <--
EP 1268555 A2 20030102 (200310) EN C07K016-28 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001072846 A2 WO 2001-US9699 20010326; AU 2001052970 A AU 2001-52970 20010326; US 2002102657 A1 Provisional US 2000-192197P 20000327, Provisional US 2000-192198P 20000327, US 2001-818247 20010326; EP 1268555 A2 EP 2001-926437 20010326, WO 2001-US9699 20010326
FDT AU 2001052970 A Based on WO 200172846; EP 1268555 A2 Based on WO 200172846
PRAI US 2000-192198P 20000327; US 2000-192197P 20000327; US 2001-818247 20010326
IC ICM C07K016-28; C12P021-04
ICS A61K031-00; A61K031-7088; A61K038-00; A61K039-395; A61K047-48; A61K048-00; A61P011-00; C07K019-00; C12N005-06
ICA C07K014-705
FS CPI

CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	3	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	2	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	0	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	0	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	4	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20030627

Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
WO 200172846	A	US 5972900	A 1995-351156/45
	PA:	(UYCA-N) UNIV CASE WESTERN RESERVE; (UYOH-N) UNIV OHIO; (OHIS) UNIV OHIO STATE; (OHIS) UNIV OHIO	
	IN:	**FERKOL, T W; HANSON, R W; PERALES, J C; DAVIS, P B; ZIADY, A**	
	A	WO 9621012	A 1996-333987/33
	PA:	(PLAN-N) PLANET BIOTECHNOLOGY INC; (UNME-N) UNITED MEDICAL & DENTAL SCHOOLS GUYS; (PLAN-N) PLANT BIOTECHNOLOGY INC; (SCRI) SCRIPPS RES INST; (HIAT-I) HIATT A C; (LEHN-I) LEHNER T; (MAJK-I) MA J K -; (MOST-I) MOSTOV K E	
	IN:	**HIATT, A C; MA, J K; LEHNER, T; MA, J K C; HEIN, M B; MOSTOV, K E; MA, J K -**	
	A	WO 9746588	A 1998-042123/04
	PA:	(REGC) UNIV CALIFORNIA	
	IN:	**MOSTOV, K E; RICHMAN-EISENSTAT, J; MOSTOV, K**	

REN LITERATURE CITATIONS UPR: 20030627

Citations by Examiner

CITING PATENT	CAT	CITED LITERATURE
WO 200172846	A	E. ECKMAN ET AL.: "In vitro transport of active alpha1-antitrypsin to the apical surface of epithelia by targeting the polymeric immunoglobulin receptor." AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY, vol. 21, no. 2, August 1999 (1999-08), pages 246-252, XP001031177 New York, NY, USA
WO 200172846	A	P. KRAJCI ET AL.: "Molecular cloning and exon-intron mapping of the gene encoding human transmembrane secretory component (the poly-Ig receptor)." EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 22, no. 9, September 1992 (1992-09), pages 2309-2315, XP000567240 Weinheim, Germany
WO 200172846	A	K. MOSTOV: "Transepithelial transport of immunoglobulins." ANNUAL REVIEW OF IMMUNOLOGY, vol. 12, 1994, pages 63-84, XP001053221 Palo Alto, CA, USA
WO 200172846	A	T. FERKOL ET AL.: "Gene transfer into respiratory epithelial cells by targeting the polymeric immunoglobulin receptor." JOURNAL OF CLINICAL INVESTIGATION, vol. 92, no. 5, November 1993 (1993-11), pages 2394-2400, XP001053217 New York, NY, USA

L113 ANSWER 2 OF 3 DPCI COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-665249 [64] DPCI
DNN N2000-493019 DNC C2000-201579
TI Quantitatively detecting ligand movement across a biological membrane, comprises contacting assay-compatible infrared fluorescent labeled ligands with a receptor.
DC B04 D16 E23 E24 S03
IN ALTSCHULER, Y; **MOSTOV, K**
PA (REGC) UNIV CALIFORNIA
CYC 21
PI WO 2000063418 A1 20001026 (200064)* EN 23p C12Q001-00 <--

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        RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
         W: AU CA JP
     AU 2000042455 A  20001102 (200107)              C12Q001-00       <--
ADT  WO 2000063418 A1 WO 2000-US10173 20000414; AU 2000042455 A AU 2000-42455
     20000414
FDT  AU 2000042455 A Based on WO 200063418
PRAI US 1999-292274   19990415
IC   ICM  C12Q001-00
     ICS  C07H019-20; C12Q001-02; C12Q001-04; C12Q001-32; G01N033-00;
          G01N033-53
FS   CPI EPI

CTCS CITATION COUNTERS
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PNC.DI    0              Cited Patents Count (by inventor)
PNC.DX    4              Cited Patents Count (by examiner)
IAC.DI    0              Cited Issuing Authority Count (by inventor)
IAC.DX    2              Cited Issuing Authority Count (by examiner)

PNC.GI    0              Citing Patents Count (by inventor)
PNC.GX    0              Citing Patents Count (by examiner)
IAC.GI    0              Citing Issuing Authority Count (by inventor)
IAC.GX    0              Citing Issuing Authority Count (by examiner)

CRC.I     0              Cited Literature References Count (by inventor)
CRC.X     3              Cited Literature References Count (by examiner)

CDP  CITED PATENTS       UPD: 20021122
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     Cited by Examiner
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     CITING PATENT    CAT    CITED PATENT     ACCNO
     ------------------------------------------------------
     WO 200063418  A  Y      US 5656449    A  1997-414585/38
                    PA:  (MOLE-N) MOLECULAR PROBES INC
                    IN:  YUE, S T
                      A     US 5658751    A  1996-251457/25
                    PA:  (MOLE-N) MOLECULAR PROBES INC
                    IN:  HAUGLAND, R P; JIN, X; JONES, L J; MILLARD, P J;
                         MOZER, T J; POOT, M; ROTH, B L; SINGER, V L; YUE, S T;
                         POOT, M E
                      Y     WO 9600902    A  1990-164056/21
                    PA:  (SIHR-I) SHIRA  K S
                    IN:  SIHRA, K S
                      Y     WO 9600902    A  1996-077582/08
                    PA:  (BIOM-N) BIOMETRIC IMAGING INC; (LEEL-I) LEE L G;
                         (WOOS-I) WOO S L
                    IN:  LEE, L G; WOO, S L
                         WO 9600902    A1 1996-077582/08
                    PA:  (BIOM-N) BIOMETRIC IMAGING INC; (LEEL-I) LEE L G;
                         (WOOS-I) WOO S L
                    IN:  LEE, L G; WOO, S L

REN  LITERATURE CITATIONS  UPR: 20010221
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     Citations by Examiner
     ---------------------

     CITING PATENT    CAT    CITED LITERATURE
     ------------------------------------------------------------------------
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WO 200063418 A CARDONE ET AL.: 'Phorbol myristate acetate-mediated stimulation of transcytosis and apical recycling in MDCK cells' THE JOURNAL OF CELL BIOLOGY vol. 124, no. 5, March 1994, pages 717 - 727, XP002930076

WO 200063418 A LIPOWSKA ET AL.: 'New near-infrared cyanine dyes for labelling of proteins' SYNTHETIC COMMUNICATIONS vol. 23, no. 21, 1993, pages 3087 - 3094, XP002930077

WO 200063418 A DATABASE CAPLUS BIOMETRIC IMAGING INC. ACC. NO. 1996194739 LEE ET AL.: 'N-heteroaromatic ion and iminium ion substituted cyanine dyes for use as fluorescence labels' & WO 96 00902 A1

L113 ANSWER 3 OF 3 DPCI COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1998-042123 [04] DPCI
DNC C1998-014108
TI Ligand that binds the stalk of a cell's polymeric immunoglobulin receptor - useful to target to, into or across mammalian epithelial cell biologically active component, e.g. nucleic acid, protein, lipid, carbohydrate, etc.
DC B04
IN **MOSTOV, K E; RICHMAN-EISENSTAT, J; MOSTOV, K**
PA (REGC) UNIV CALIFORNIA
CYC 77
PI WO 9746588 A1 19971211 (199804)* EN 42p C07K016-00 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN YU
AU 9730632 A 19980105 (199821) C07K016-00 <--
EP 934338 A1 19990811 (199936) EN C07K016-00 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1221428 A 19990630 (199944) C07K016-00 <--
US 6042833 A 20000328 (200023) A61K038-16 <--
JP 2000511432 W 20000905 (200047) 46p C12N015-09 <--
AU 728587 B 20010111 (200108) C07K016-00 <--
IL 127238 A 20010724 (200147) C07K016-00 <--
US 6340743 B1 20020122 (200208) C07K016-28 <--
RU 2191781 C2 20021027 (200281) C07K016-42 <--
ADT WO 9746588 A1 WO 1997-US7944 19970514; AU 9730632 A AU 1997-30632 19970514; EP 934338 A1 EP 1997-925515 19970514, WO 1997-US7944 19970514; CN 1221428 A CN 1997-195238 19970514; US 6042833 A Provisional US 1996-18958P 19960604, US 1997-856383 19970514; JP 2000511432 W WO 1997-US7944 19970514, JP 1998-500584 19970514; AU 728587 B AU 1997-30632 19970514; IL 127238 A IL 1997-127238 19970514; US 6340743 B1 Provisional US 1996-18958P 19960604, Div ex US 1997-856383 19970514, US 1999-475088 19991230; RU 2191781 C2 WO 1997-US7944 19970514, RU 1999-100279 19970514
FDT AU 9730632 A Based on WO 9746588; EP 934338 A1 Based on WO 9746588; JP 2000511432 W Based on WO 9746588; AU 728587 B Previous Publ. AU 9730632, Based on WO 9746588; US 6340743 B1 Div ex US 6042833; RU 2191781 C2 Based on WO 9746588
PRAI US 1996-18958P 19960604; US 1997-856383 19970514; US 1999-475088 19991230
IC ICM A61K038-16; C07K016-00; C07K016-28; C07K016-42; C12N015-09
ICS A61K039-385; A61K039-395; C07K016-46; C12N015-13
FS CPI

EXF EXAMINER'S FIELD OF SEARCH UPE: 20020731

NCL US 6042833 A 20000328

424/134.100; 424/185.100; 424/193.100; 530/380; 530/395; 530/403
US 6340743 B1 20020122
000/424.130 .1; 000/424.132 .1; 000/424.133 1-1351; 000/424.139 .1;
000/424.141 .1; 000/424.143 .1; 000/424.178 .1; 000/424.182 .1;
000/424.183 .1; 000/530.387 .1; 000/530.387 .3; 000/530.387 .5;
000/530.387 .9; 000/530.388 .1; 000/530.388 .22; 000/530.389 .1;
000/530.391 .1; 000/530.391 .3; 000/530.391 .7

CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	0	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	0	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	2	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	2	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	34	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20020731

Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
US 6042833	A	No Citations	
US 6340743	B1	No Citations	
WO 9746588	A	No Citations	

REN LITERATURE CITATIONS UPR: 20020731

Citations by Examiner

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US 6042833	A	Mazanec et al., J. Virol. 69(2):1339-1343 (Feb. 1995).
US 6042833	A	Williams, G., Tibtech 6:36-42 (Feb. 1988).
US 6042833	A	Hudson, L. et al. (ed), Practical Immunology, 2nd edition, pp. 192-202, 1980.
US 6042833	A	Solari, R. et al., J. Biol. Chem. 260:1141-1145, Antibodies recognizing differen domains of the polymeric immunoglobulin receptor, 1985.
US 6042833	A	Eiffert et al., Physiol. Chem. 365:1489-1495 (1984).
US 6042833	A	Solari et al., J. Histochemistry and Cytochemistry 34(1):17-23 (1986).
US 6042833	A	Breitfeld et al., J. Cell Biology 109:475-486 (1989).
US 6042833	A	Piskurich et al., Journal of Immunology 154:1735-1747 (1995).
US 6042833	A	Ferkol et al., J. Clin. Invest. 95:493-502 (1995).
US 6042833	A	Wu et al., J. Biol. Chem. 262:4429-4432 (1987).
US 6042833	A	Breitfeld et al., Methods in Cell Biology 32:329-337 (1989).

US 6042833	A	Mostov et al., Ann. Rev. Immunol. 12:63-84 (1994).
US 6042833	A	Ferkol et al., J. Clin. Invest. 92:2394-2400 (Nov. 1993).
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US 6340743	B1	Mostov, Keith E., et al., Nature, 308(5954):37-43 (Mar. 1, 1984).
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US 6340743	B1	Solari et al., J. Histochemistry and Cytochemistry 34(1):17-23 (1986).
US 6340743	B1	Ferkol et al., J. Clin. Invest. 92:2394-2400 (Nov. 1993).
US 6340743	B1	Mostov et al., Ann. Rev. Immunol. 12:63-84 (1994).
US 6340743	B1	Ferkol et al., J. Clin. Invest. 95:493-502 (1995).
US 6340743	B1	Wu et al., J. Biol. Chem. 262:4429-4432 (1987).
US 6340743	B1	Breitfeld et al., Methods in Cell Biology 32:329-337 (1989).
US 6340743	B1	Eiffert et al., Physiol. Chem. 365:1489-1495 (1984).
US 6340743	B1	Mazanec et al., J. Virol. 69(2):1339-1343 (Feb. 1995).
US 6340743	B1	Williams, G., TIBTECH 6:36-42 (Feb. 1988).
US 6340743	B1	Hudson, L., et al. (ed), Practical Immunology, 2nd edition, pp. 192-202 (1980).
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WO 9746588	A	J. VIROL., February 1995, Vol. 69, No. 2, MAZANEC et al., "Intracellular Neutralization of Influenza Virus by Immunoglobulin A Anti-hemagglutinin Monoclonal Antibodies", pages 1339-1343.
WO 9746588	A	TIBTECH, February 1988, Vol. 6, WILLIAMS G., "Novel Antibody Reagents: Production and Potential", pages 36-42.
WO 9746588	A	J. HISTOCHEMISTRY CYTOCHEMISTRY, 1986, Vol. 34, No. 1, SOLARI et al., "Distribution and Processing of the Polymeric Immunoglobulin Receptor in the Rat Hepatocyte: Morphological and Biochemical Characterization of Subcellular Fractions", pages 17-23.
WO 9746588	A	J. CLIN. INVEST., November 1993, Vol. 92, FERKOL et al., "Gene Transfer into Respiratory Epithelial Cells by Targeting the Polymeric Immunoglobulin Receptor", pages 2394-2400.
WO 9746588	A	ANN. REV. IMMUNOL., 1994, Vol. 12, MOSTOV et al., "Transepithelial Transport of Immunoglobulins", pages 63-84.

CGP CITING PATENTS UPG: 20021009

Cited by Examiner

CITED PATENT	CAT	CITING PATENT	ACCNO
WO 9746588	A X	WO 200047611 A2	2000-549134/52

PA: (DGIB-N) DGI BIOTECHNOLOGIES; (OKLA-N) OKLAHOMA MEDICAL RES FOUND; (TEXA) UNIV TEXAS SYSTEM; (DGIB-N) DGI BIOTECHNOLOGIES INC
IN: **CAPRA, J D; HEXHAM, J M; MANDECKI, W; WHITE, K**

WO 9746588 A1 US 6207195 B1 1999-080847/01
PA: (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE; (UYJO) UNIV JOHNS HOPKINS
IN: **LEONG, K; RUBENSTEIN, R; WALSH, S; ZEITLIN, P; LEONG, K W**

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FILE 'HCAPLUS' ENTERED AT 08:09:40 ON 23 JUL 2003
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FILE COVERS 1907 - 23 Jul 2003 VOL 139 ISS 4
FILE LAST UPDATED: 22 Jul 2003 (20030722/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs tot l145

L145 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:519374 HCAPLUS
DN 135:121191
TI Bifunctional molecules for delivery of therapeutics
IN Davis, Pamela B.; Ferkol, Thomas W., Jr.; Eckman, Elizabeth
PA Case Western Reserve University, USA
SO U.S., 34 pp., Cont.-in-part of U.S. 6,072,041.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 6261787	B1	20010717	US 1999-264032	19990308	
	US 5972900	A	19991026	US 1996-655705	19960603	<--
	US 5972901	A	19991026	US 1996-656906	19960603	
	US 6072041	A	20000606	US 1997-957333	19971024	
	WO 2000053623	A1	20000914	WO 2000-US5930	20000308	
	W: AU, CA, JP					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	EP 1165597	A1	20020102	EP 2000-913784	20000308	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2003522117	T2	20030722	JP 2000-604058	20000308	
PRAI	US 1996-655705	A2	19960603			

US 1996-656906 A2 19960603
US 1997-957333 A2 19971024
US 1994-216534 B2 19940323
WO 1995-US3677 A1 19950323
US 1999-264032 A 19990308
WO 2000-US5930 W 20000308

AB A bifunctional mol. consisting of a therapeutic mol. and a **ligand** which specifically binds a transcytotic receptor can be transported specifically from the basolateral surface of epithelial cells to the apical surface. This approach provides the ability to deliver a therapeutic mol. directly to the apical surface of the epithelium, by targeting the transcytotic receptor with an appropriate **ligand**. Thus, the highest concn. of the therapeutic mol. will be at the apical surface, where it can have the greatest therapeutic effect.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L145 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:573823 HCAPLUS
DN 133:176176
TI **Polymeric immunoglobulin receptor** (**pIgR**)-binding domains and methods of use therefor
IN Capra, J. Donald; White, Kendra; Hexham, J. Mark; Mandecki, Wlodeck
PA Oklahoma Medical Research Foundation, USA; Board of Regents, the University of Texas System; Dgi Biotechnologies
SO PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000047611	A2	20000817	WO 2000-US3650	20000211 <--
WO 2000047611	A3	20001130		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1151000	A2	20011107	EP 2000-906030	20000211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539771	T2	20021126	JP 2000-598527	20000211
PRAI US 1999-119932P	P	19990212		
WO 2000-US3650	W	20000211		

AB The present invention identifies a domain located in the C.alpha.3 domain of IgA that is responsible for targeting of the **polymeric Ig receptor** (**pIgR**) and transport of the antibody to the mucosal epithelium. This **pIgR**-binding domain may be used to target a wide variety of compns., including proteins, nucleic acids, drugs and diagnostic agents, to the mucosal surface. Other more specific targeting agents may be used in conjunction with the **pIgR**-binding domain to define further the ultimate localization of the complexes in the body. Treatment of a large no. of disease conditions such as viral, fungal and bacterial infections, as well as cancer, may be improved through the use of a **pIgR**-binding domain.

L145 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:381472 HCAPLUS

DN 133:3719
TI Antibody fusion proteins for targeting apical epithelium
IN Davis, Pamela B.; Ferkol, Thomas; Eckman, Elizabeth; Schreiber, John; Luk, John M.
PA Case Western Reserve University, USA
SO U.S., 24 pp., Cont.-in-part of U.S. 655,705.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 6072041	A	20000606	US 1997-957333	19971024	
	US 5972900	A	19991026	US 1996-655705	19960603	<--
	US 5972901	A	19991026	US 1996-656906	19960603	
	US 6261787	B1	20010717	US 1999-264032	19990308	
	US 6287817	B1	20010911	US 2000-559393	20000426	
PRAI	US 1996-655705	A2	19960603			
	US 1996-656906	A2	19960603			
	US 1994-216534	B2	19940323			
	WO 1995-US3677	A1	19950323			
	US 1997-957333	A2	19971024			

AB The authors disclose the construction and characterization of single-chain antibody fusion proteins directed at the **polymeric Ig receptor** (**pIgR**). Such constructs have the ability to deliver a therapeutic protein directly to the apical surface of the epithelium. In one example, a fusion protein with .alpha.1-antitrypsin was transported to the apical surface of MDCK cells expressing a transgene for **pIgR**.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L145 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:686690 HCAPLUS
DN 131:327493
TI Serpin enzyme complex receptor-mediated gene transfer
IN Ferkol, Thomas W., Jr.; Davis, Pamela B.; Ziady, Assem-galal
PA Case Western Reserve University, USA
SO U.S., 81 pp., Cont.-in-part of U.S. Ser. No. 655,705.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5972901	A	19991026	US 1996-656906	19960603	
	WO 9525809	A1	19950928	WO 1995-US3677	19950323	
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT					
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5972900	A	19991026	US 1996-655705	19960603	<--
	WO 9746100	A1	19971211	WO 1997-US9858	19970603	
	W: AU, CA, JP					
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	AU 9733044	A1	19980105	AU 1997-33044	19970603	
	AU 720223	B2	20000525			
	EP 1006797	A1	20000614	EP 1997-928891	19970603	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					

	JP 2000512140	T2	20000919	JP 1998-500875	19970603
	US 6072041	A	20000606	US 1997-957333	19971024
	US 6261787	B1	20010717	US 1999-264032	19990308
	US 6287817	B1	20010911	US 2000-559393	20000426
PRAI	US 1994-216534	B2	19940323		
	WO 1995-US3677	A1	19950323		
	US 1996-655705	A2	19960603		
	US 1996-656906	A	19960603		
	WO 1997-US9858	W	19970603		
	US 1997-957333	A2	19971024		

AB Nucleic acids are compacted, substantially without aggregation, to facilitate their uptake by target cells of an organism to which the compacted material is administered. The nucleic acids may achieve a clin. effect as a result of gene expression, hybridization to endogenous nucleic acids whose expression is undesired, or site-specific integration so that a target gene is replaced, modified or deleted. The targeting may be enhanced by means of a target cell-binding moiety. The nucleic acid is preferably compacted to a condensed state.

RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L145 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:547711 HCAPLUS
DN 131:285105
TI In vitro transport of active .alpha.1-antitrypsin to the apical surface of epithelia by targeting the **polymeric immunoglobulin receptor**
AU **Eckman, Elizabeth A.**; Mallender, William D.; Szegletes, Tivadar; Silski, Catherine L.; Schreiber, John R.; Davis, Pamela B.; Ferkol, Thomas W.
CS Department of Pediatrics, Case Western Reserve University, Cleveland, OH, 44106, USA
SO American Journal of Respiratory Cell and Molecular Biology (**1999**), **21**(**2**), **246**-252
CODEN: AJRBEL; ISSN: 1044-1549
PB American Lung Association
DT Journal
LA English
AB In cystic fibrosis (CF), the intense host inflammatory response to chronic infection largely accounts for the progressive pulmonary disease, and ultimately death. Neutrophils are the prominent inflammatory cells in the lungs of patients with CF, and large amts. of neutrophil elastase (NE) are released during phagocytosis. Besides having direct effects on structural elastin, NE stimulates the release of proinflammatory mediators from the respiratory epithelium and is a potent secretagogue. Therapeutic use of elastase inhibitors in CF has been complicated by difficulties in delivery to the crit. site in the airway-the surface of the epithelium. We describe a unique strategy to protect the respiratory epithelial cell surface directly by capitalizing on the nondegradative transcytotic pathway of the **polymeric Ig receptor** (**pIgR**). A recombinant fusion protein was constructed consisting of an antihuman **pIgR** single-chain Fv (scFv) antibody linked to human .alpha.1-antitrypsin (A1AT), an inhibitor of NE. The recombinant scFv-A1AT fusion protein bound specifically to the **pIgR** on the basolateral surface of an epithelial cell monolayer, and was transported and released into the apical medium where the A1AT domain was capable of forming an inactivation complex with NE. Thus, A1AT linked to an antihuman **pIgR** scFv was delivered in **receptor**-specific fashion from the basolateral to apical surface and was released as an active antiprotease, indicating that it is feasible to deliver therapeutic proteins to the apical surface of epithelia by targeting the **pIgR**

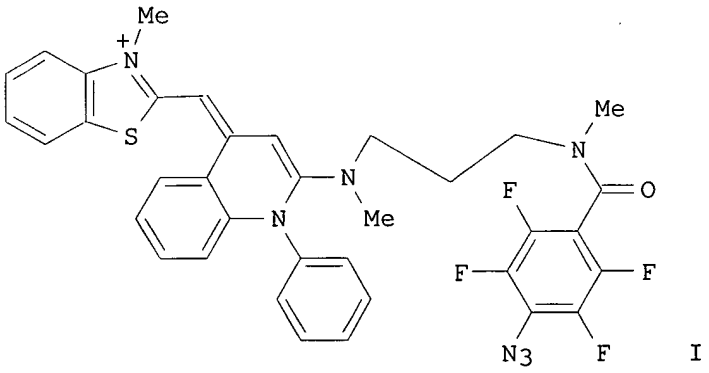
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L145 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:69867 HCAPLUS
DN 130:150635
TI Chemically reactive unsymmetrical cyanine dyes and their conjugates
IN Haugland, Richard P.; Singer, Victoria L.; Yue, Stephen T.; Millard, Paul J.
PA Molecular Probes, Inc., USA
SO U.S., 27 pp., Cont.-in-part of U.S. 5,658,751.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5863753	A	19990126	US 1997-914439	19970819
	US 5658751	A	19970819	US 1994-331031	19941027 <--
PRAI	US 1994-331031	A2	19941027		
	US 1993-47683	B2	19930413		
	US 1994-90890	A2	19940712		

OS MARPAT 130:150635
GI



I

AB The invention comprises cyanine dyes, in particular chem. reactive dyes, conjugates of reactive cyanine dyes, the non-covalent complexes of nucleic acids with the dyes and dye-conjugates of the invention, and a method of forming a nucleic acid complex with the dyes and dye-conjugates of the present invention. The dyes of the invention are useful for the prepn. of dye-conjugates. The presence of a reactive group on the unsym. cyanine dyes of the invention facilitates their covalent conjugation to a variety of substances, both biol. and synthetic. Double-stranded DNA was photoaffinity labeled with I (prepn. given).
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L145 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:7813 HCAPLUS
DN 130:71529
TI Therapeutic nanospheres containing sodium 4-phenylbutyrate for treatment of cystic fibrosis by CFTR gene therapy
IN Walsh, Scott; Rubenstein, Ronald; Zeitlin, Pamela; Leong, Kam
PA Johns Hopkins University School of Medicine, USA
SO PCT Int. Appl., 24 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9856370	A2	19981217	WO 1998-US11880	19980611
WO 9956370	A3	19990401		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2303268	AA	19981217	CA 1998-2303268	19980611
AU 9880624	A1	19981230	AU 1998-80624	19980611
AU 749032	B2	20020620		
EP 989849	A2	20000405	EP 1998-928941	19980611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6207195	B1	20010327	US 1998-95882	19980611 <--
JP 2002506436	T2	20020226	JP 1999-503069	19980611
PRAI US 1997-49497P	P	19970613		
WO 1998-US11880	W	19980611		

AB 4-Phenylbutyrate exerts many beneficial biol. effects. It appears to induce the transcription of certain promoters, as well as having a remedial effect on proteins which are aberrantly localized within the cell. In addn., it appears to cause cells to developmentally differentiate. The present invention provides nanosphere formulations of 4-phenylbutyrate and other drugs which remediate defective protein localization intracellularly and can be used for treating cystic fibrosis. These formulations permit lower concns. of drugs to be administered, providing both cost and safety benefits.

L145 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:574469 HCAPLUS
DN 127:231608
TI Substituted unsymmetrical cyanine dyes with selected permeability
IN Yue, Stephen T.; Singer, Victoria L.; Roth, Bruce L.; Mozer, Thomas J.; Millard, Paul J.; Jones, Laurie J.; Jin, Xiaokui; Haugland, Richard P.
PA Molecular Probes, Inc., USA
SO U.S., 58 pp., Cont.-in-part of U.S. 5,436,134.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 8

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5658751	A	19970819	US 1994-331031	19941027 <--
WO 9613552	A2	19960509	WO 1995-US13706	19951027
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9539672	A1	19960523	AU 1995-39672	19951027
AU 714890	B2	20000113		
WO 9613552	A3	19960711	WO 1995-EP13706	19951027
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 740689	A1	19961106	EP 1995-937613	19951027
EP 740689	B1	20020130		
R: AT, BE, CH, DE, FR, GB, LI, NL				
JP 09507879	T2	19970812	JP 1995-514689	19951027

	AT 212653	E	20020215	AT 1995-937613	19951027
	US 5863753	A	19990126	US 1997-914439	19970819
PRAI	US 1993-47683	B2	19930413		
	US 1994-90890	A2	19940712		
	US 1994-331031	A	19941027		
	WO 1995-US13706	W	19951027		

OS MARPAT 127:231608

AB The invention describes the prepn. and use of fluorescent stains for nucleic acids derived from unsym. cyanine dyes comprising a substituted benzazolium ring system linked by a methine bridge to a pyridinium or quinolinium ring system having at least one substituent on the pyridinium or quinolinium ring that contains a heteroatom. The presence of the heteroatom-contg. substituent results in higher sensitivity to oligonucleotides and larger nucleic acid polymers in a wide range of cells and gels, and for use in anal. of cell structure, membrane integrity or function. Thus, Dye 640 was prepd. by the methylation of 2-chloro-3-methylquinoline followed by the reaction of the intermediate iodide with 3-methyl-2-methylthiobenzothiazolinium tosylate in CH2Cl2 in the presence of 1 equiv. of NEt3. The use of these dyes in the detection of DNA in electrophoretic gels was demonstrated.

L145 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:537669 HCAPLUS

DN 125:187585

TI Immunoglobulin fusion product with immunoglobulin receptor that protects Ig in mucosal environment, cDNA sequences, transgenic plants, and dental carie prevention

IN Hiatt, Andrew C.; Ma, Julian K.-C.; Lehner, Thomas

PA Planet Biotechnology, Inc., USA; United Medical and Dental Schools of Guy's and St. Thomas's Hospital

SO PCT Int. Appl., 154 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9621012	A1	19960711	WO 1995-US16889	19951227 <--
	W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SG				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6046037	A	20000404	US 1995-434000	19950504
	AU 9646088	A1	19960724	AU 1996-46088	19951227
	AU 722668	B2	20000810		
	EP 807173	A1	19971119	EP 1995-944237	19951227
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PRAI	US 1994-367395	A	19941230		
	US 1995-434000	A	19950504		
	WO 1995-US16889	W	19951227		

AB The Igs of the present invention are useful therapeutic Igs against mucosal pathogens such as S. mutans. The Igs contain a protection protein that protects the Igs in the mucosal environment. The invention also includes the greatly improved method of producing Igs in plants by producing the protection protein in the same cell as the other components of the Igs. The components of the Ig and assembled at a much improved efficiency. The method of the invention allows the assembly and high efficiency prodn. of such complex mols. The invention also contemplates the prodn. of Igs contg. protection proteins in a variety of cells, including plant cells, that can be selected for useful addnl. properties. The use of Igs contg. protection proteins as therapeutic antibodies against mucosal and other pathogens is also contemplated.

L145 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:443964 HCAPLUS

DN 125:81256
TI Substituted unsymmetrical cyanine dyes with selected permeability
IN Yue, Stephen T.; Singer, Victoria L.; Roth, Bruce L.; Mozer, Thomas J.; Millard, Paul J.; Jones, Laurie J.; Jin, Xiaokui; Haugland, Richard P.; Poot, Martin
PA Molecular Probes, Inc., USA
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9613552	A2	19960509	WO 1995-US13706	19951027	
	W: AU, CA, JP					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5658751	A	19970819	US 1994-331031	19941027	<--
	AU 9539672	A1	19960523	AU 1995-39672	19951027	
	AU 714890	B2	20000113			
	EP 740689	A1	19961106	EP 1995-937613	19951027	
	EP 740689	B1	20020130			
	R: AT, BE, CH, DE, FR, GB, LI, NL					
	JP 09507879	T2	19970812	JP 1995-514689	19951027	
	AT 212653	E	20020215	AT 1995-937613	19951027	
PRAI	US 1994-331031	A	19941027			
	US 1993-47683	B2	19930413			
	US 1994-90890	A2	19940712			
	WO 1995-US13706	W	19951027			

OS MARPAT 125:81256
AB The invention describes the prepn. and use of fluorescent stains for nucleic acids derived from unsym. cyanine dyes comprising a substituted benzazolium ring system linked by a methine bridge to a pyridinium or quinolinium ring system. The cyanine dyes of the invention possess a high sensitivity to oligonucleotides and larger nucleic acid polymers in a wide range of cells and gels, and are useful for the anal. of cell structure, membrane integrity or function, and detn. of cell cycle distribution.

L145 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:194739 HCAPLUS
DN 124:225822
TI N-**heteroaromatic** ion and **iminium** ion substituted **cyanine** dyes for use as **fluorescence** labels
IN **Lee, Linda G.**; Woo, Sam L.
PA Biometric Imaging, Inc., USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9600902	A1	19960111	WO 1995-US8778	19950629	<--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA					
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5453505	A	19950926	US 1994-268852	19940630	
	AU 9530085	A1	19960125	AU 1995-30085	19950629	
	EP 769145	A1	19970423	EP 1995-926272	19950629	
	R: AT, BE, CH, DE, ES, FR, GB, IE, IT, LI, LU, NL, SE					

PRAI US 1994-268852 19940630
US 1995-388607 19950214
WO 1995-US8778 19950629
OS MARPAT 124:225822
GI For diagram(s), see printed CA Issue.
AB The present invention relates to **iminium** ion-substituted **cyanine** dyes having a **fluorescence** absorbance of between about 500 and 900 nm, a reduced tendency to aggregate and enhanced photostability. The **cyanine** dyes of the present invention are represented by formula I where n is 0, 1, 2 or 3; R1 and R2 are taken together to form an arom. ring or a fused polycyclic arom. ring; R3 and R4 are taken together to form an arom. ring or a fused polycyclic arom. ring; R5 and R6 are independently selected from the group consisting of (CH2)pX where p is 1-18 and X is a functional group that reacts with amino, hydroxy and sulfhydryl nucleophiles; R7 and R8 are independently selected from the group consisting of H, C1-C10 alkyl groups and where R7 and R8 are taken together to form a 5- or 6-membered heterocyclic ring; R9 are each independently selected from the group consisting of H, alkyl and where >1 R9 are taken together to form a 5- or 6-membered ring; Y is selected from the group consisting of C(CH3)2, S, O and Se; and Z is selected from the group consisting of C(CH3)2, S, O and Se. The present invention also relates to a method for using the **cyanine** dyes of the present invention to **fluorescent** label mols., particularly biomols. such as antibodies, DNA, carbohydrates and cells.

L145 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:963703 HCAPLUS
DN 123:332097
TI Compacted nucleic acids and their delivery to cells for gene therapy
IN Hanson, Richard W.; Perales, Joseph C.; Ferkol, Thomas W., Jr.
PA Ohio University, USA
SO PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9525809	A1	19950928	WO 1995-US3677	19950323
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2186118	AA	19950928	CA 1995-2186118	19950323
	AU 9521276	A1	19951009	AU 1995-21276	19950323
	AU 696455	B2	19980910		
	EP 752005	A1	19970108	EP 1995-914173	19950323
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10503469	T2	19980331	JP 1995-524826	19950323
	US 5972900	A	19991026	US 1996-655705	19960603 <--
	US 5972901	A	19991026	US 1996-656906	19960603
	US 5877302	A	19990302	US 1997-716415	19970212
	US 6200801	B1	20010313	US 1998-217847	19981221
PRAI	US 1994-216534	A	19940323		
	WO 1995-US3677	W	19950323		
	US 1996-655705	A2	19960603		
	US 1996-655706	A2	19960603		
	US 1996-656096	A3	19960603		

AB Nucleic acids are compacted, substantially without aggregation, to facilitate their uptake by target cells of an organism to which the

compacted material is administered. The nucleic acids may achieve a clin. effect as a result of gene expression, hybridization to endogenous nucleic acids whose expression is undesired, or site-specific integration so that a target gene is replaced, modified or deleted. The targeting may be enhanced by means of a target-cell-binding moiety. The nucleic acid is preferably compacted to a condensed state.

L145 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:875020 HCAPLUS
DN 124:32008
TI N-**Heteroaromatic** ion- and **iminium** ion-substituted **cyanine** dyes and their use as **fluorescent** labels
IN **Lee, Linda G.**; Woo, Sam L.
PA Biometric Imaging, Inc., USA
SO U.S., 18 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5453505	A	19950926	US 1994-268852	19940630
	WO 9600902	A1	19960111	WO 1995-US8778	19950629 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2194150	AA	19960111	CA 1995-2194150	19950629
	AU 9530085	A1	19960125	AU 1995-30085	19950629
	EP 769145	A1	19970423	EP 1995-926272	19950629
	R: AT, BE, CH, DE, ES, FR, GB, IE, IT, LI, LU, NL, SE				
PRAI	US 1994-268852		19940630		
	US 1995-388607		19950214		
	WO 1995-US8778		19950629		

OS MARPAT 124:32008
GI For diagram(s), see printed CA Issue.
AB The dyes having a **fluorescence** absorbance between 500 and 900 nm, a reduced tendency to aggregate, and enhanced photostability. They are represented by the formula I (A and B are arom. rings or fused polycyclic arom. rings; each R = H, alkyl, or 2 R together form a 5- or 6-membered ring; R1, R2 = (CH2)pX; R3, R4 = H, C1-10 alkyl, or R3R4 completes a 5- or 6-membered heterocyclic ring; X is a functional group that reacts with amino, OH, and SH nucleophiles; Z, Z1 = CMe2, S; m, n = 0-3; p = 1-18). Thus, 2,3,3-trimethylindoline was alkylated with Br(CH2)5CO2H, condensed 2:1 with II, and the meso-Cl **cyanine** treated with 4-(dimethylamino)pyridine to give I [A = B = benzo, the R on the C atoms to either side of the meso C combine to form (CH2)3, the remaining R = H, R1 = R2 = (CH2)5CO2H, R3R4 = :CHC(NMe2):CH, Z = Z1 = CMe2, m = n = 1], absorption .lambda.max 786 nm, which was monoesterified with N-hydroxysuccinimide and used to label mouse IgG.

L145 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:874985 HCAPLUS
DN 123:266187
TI Method of encapsulating biological substances in microspheres
IN Tresco, Patrick A.; Mills, John F.
PA Brown University Research Foundation, USA
SO U.S., 6 pp.
CODEN: USXXAM
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5453368	A	19950926	US 1993-113778	19930827
	US 5656469	A	19970812	US 1995-514780	19950814 <--
PRAI	US 1993-113778		19930827		

AB A method for encapsulating a biol. substance in biocompatible microcapsules, comprises (1) maintaining a coat-forming liq. film sheet comprising a polymer in an org. solvent, (2) causing droplets comprising biol. substance in an aq. medium to pass through the sheet to form microcapsules comprising cores of the droplets coated by the liq. film, and (3) permitting the microcapsules to pass through the sheet so that a portion of the polymer ppts. in the presence of water in the droplets while evapg. a portion of the solvent to form a continuous permeable polymer coating of sufficient structural integrity so that the microcapsules are self-supporting. A suitable app. is illustrated for performing the method of the present invention. Microencapsulation of PC 12 cells using polyacrylonitrile in DMF was demonstrated. A sample of the microcapsules was placed in culture and at the end of 6 wks, the microcapsules showed viable cells.

L145 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:362852 HCAPLUS
DN 122:158173
TI Molecular cloning of the mouse **polymeric Ig receptor**. Functional regions of the molecule are conserved among five mammalian species
AU **Piskurich, Janet F.**; Blanchard, May H.; Youngman, Kenneth R.; France, John A.; Kaetzel, Charlotte S.
CS Inst. Pathol., Case Western Reserve Univ., Cleveland, OH, 44106, USA
SO Journal of Immunology (**1995**), **154**(4), **1735**-47
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Transcytosis of **polymeric Ig** (pIg) by mucosal epithelial cells is mediated by the **polymeric Ig receptor** (**pIgR**). Here the authors describe the characterization of a 3095-bp mouse **pIgR** cDNA, which encodes a protein of 771 amino acids. Northern blot anal. detected a single mouse **pIgR** transcript of 3.9 kb, expressed at high levels in small intestine and liver, and at low levels in lung. Alignment of the amino acid sequences of mouse, rat, human, bovine, and rabbit **pIgR** revealed that functional regions of the mol. are conserved across species. In the extracellular region, conserved motifs include: a 23-amino acid pIg-binding site; 11 intradomain disulfide bonds, consensus sites for N-glycosylation, and a putative cleavage site at which the extracellular region of **pIgR** (secretory component) is released from the plasma membrane. A 10-amino acid sequence within the transmembrane region is highly conserved, possibly reflecting a mechanism for transmitting signals from the extracellular region to the cytoplasmic tail. Conversion within the cytoplasmic tail of **pIgR** is clustered in motifs that mediate polarized sorting, endocytosis, and transcytosis.

L145 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:349785 HCAPLUS
DN 122:124430
TI Gene transfer into the airway epithelium of animals by targeting the **polymeric immunoglobulin receptor**
AU **Ferkol, Thomas**; Perales, Jose C.; Eckman, Elizabeth; Kaetzel, Charlotte S.; Hanson, Richard W.; Davis, Pamela B.

CS Dep. Pediatr., Rainbow Babies Child. Hosp., Cleveland, OH, 44106, USA
SO Journal of Clinical Investigation (**1995**), **95**(2), **493**-502
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
AB Genes of interest can be targeted specifically to respiratory epithelial cells in intact animals with high efficiency by exploiting the **receptor**-mediated endocytosis of the **polymerin Ig receptor**. A DNA carrier, consisting of the Fab portion of polyclonal antibodies raised against rat secretory component covalently linked to poly-L-lysine, was used to introduce plasmids contg. different reporter genes into airway epithelial cells in vivo. We obsd. significant levels of luciferase enzyme activity in protein exts. from the liver and lung, achieving max. values of 13,795 .+-. 4,431 and 346,954 .+-. 199,120 integrated light units (ILU) per mg of protein ext., resp. No luciferase activity was detected in spleen or heart, which do not express the **receptor**. Transfections using complexes consisting of an irrelevant plasmid (pCMV lacZ) bound to the bona fide carrier based on an irrelevant Fab fragment tissues resulted in background levels of luciferase activity in all tissues examd. Thus, only tissues that contain cells bearing the **polymeric Ig receptor** are transfected, and transfection cannot be attributed to the nonspecific uptake of an irrelevant carrier-DNA complex. Specific mRNA from the luciferase gene was also detected in the lungs of transfected animals. To det. which cells in the lung are transfected by this method, DNA complexes were prepd. contg. expression plasmids with genes encoding the bacterial .beta.-galactosidase or the human interleukin 2 **receptor**. Expression of these genes were localized to the surface epithelium of the airways with submucosal glands, and not the bronchioles and alveoli. **Receptor**-mediated endocytosis can be used to introduce functional genes into the respiratory epithelium of rats, and may be a useful technique for gene therapy targeting the lung.

L145 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:335992 HCAPLUS
DN 122:103619
TI Intracellular neutralization of influenza virus by immunoglobulin A anti-hemagglutinin monoclonal antibodies
AU **Mazanec, Mary B.**; Coudret, Christina L.; Fletcher, David R.
CS Dep. Med. Pathol., Case Western Reserve Univ., Cleveland, OH, 44106, USA
SO Journal of Virology (**1995**), **69**(2), **1339**-43
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB Traditionally, IgA was thought to neutralize virus by forming complexes with viral attachment proteins, blocking attachment of virions to host epithelial cells. Recently we have proposed an intracellular action for dimeric IgA, which is actively transported through epithelial cells by the **polymeric Ig receptor** (**pIgR**), in that it may be able to bind to newly synthesized viral proteins within the cell, preventing viral assembly. To this effect, we have previously demonstrated that IgA monoclonal antibodies against Sendai virus, a parainfluenza virus, colocalize with the viral hemagglutinin-neuraminidase protein within infected epithelial cells and reduce intracellular viral titers. Here we det. whether IgA can interact with influenza virus hemagglutinin (HA) protein within epithelial cells. Polarized monolayers of Madin-Darby canine kidney epithelial cells expressing the **pIgR** were infected on their apical surfaces with influenza virus A/Puerto Rico/8-Mount Sinai. **Polymeric** IgA anti-HA, but not IgG anti-HA,

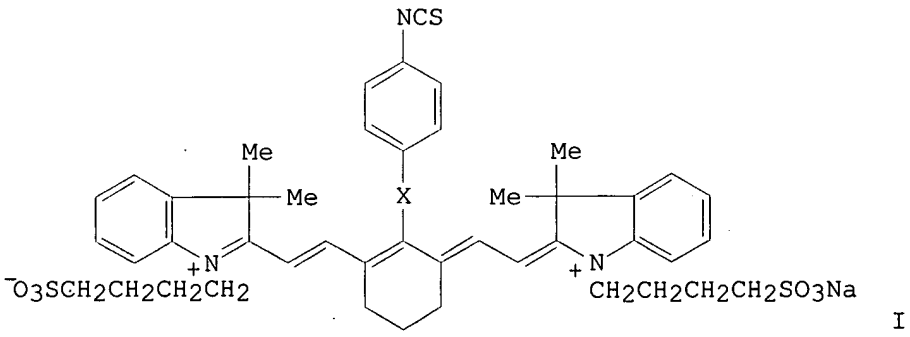
delivered to the basolateral surface colocalized with HA protein within the cell by immunofluorescence. Compared with those of controls, viral titers were reduced in the supernatants and cell lysates from monolayers treated with anti-HA IgA but not with anti-HA IgG. Furthermore, the addn. of anti-IgA antibodies to supernatants did not interfere with the neutralizing activity of IgA placed in the basal chamber, indicating that IgA was acting within the cell and not in the extracellular medium to interrupt viral replication. Thus, these studies provide addnl. support for the concept that IgA can inhibit replication of microbial pathogens intracellularly.

L145 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:296085 HCAPLUS
DN 120:296085
TI Transepithelial transport of immunoglobulins
AU **Mostov, Keith E.**
CS Dep. Anat., Univ. California, San Francisco, CA, 94143-0452, USA
SO Annual Review of Immunology (**1994**), **12**, **63**
-84
CODEN: ARIMDU; ISSN: 0732-0582
DT Journal; General Review
LA English
AB A review with 90 refs. **Igs** are transported across a variety of epithelial tissues. The best studied example of this is the transport of **polymeric** IgA and IgM by the **polymeric Ig receptor** (**pIgR**) across many types of epithelial cells. Transcytosis may be regulated by the heterotrimeric Gs protein, protein kinase C and calmodulin. IgG is transcytosed from the apical to basolateral surface in several epithelial tissues such as the placenta and the small intestine of newborn rats. The **receptor** for intestinal transport of IgG is structurally similar to class I MHC mols.

L145 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:130640 HCAPLUS
DN 120:130640
TI Phorbol myristate acetate-mediated stimulation of transcytosis and apical recycling in MDCK cells
AU **Cardone, Michael H.**; Smith, Bradley L.; Song, Wenxia; Mochley-Rosen, Daria; **Mostov, Keith E.**
CS Dep. Anat., Univ. California, San Francisco, CA, 94143-0452, USA
SO Journal of Cell Biology (**1994**), **124**(**5**), **717**-28
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
AB Phorbol myristate acetate (PMA) stimulates transcytosis of the **polymeric Ig receptor** (**pIgR**) in MDCK cells. Apical release of pre-endocytosed **ligand** (dimeric IgA) bound to the **pIgR** can be stimulated 2-fold within 7 min of addn. of PMA while recycling of the **ligand** from the basal surface is not affected. In addn., apical surface delivery of **pIgR** and cleavage of its ectodomain to secretory component (SC) is also stimulated by PMA. The recycling of apically internalized **ligand** back to the apical surface is similarly stimulated. These results suggest that the stimulation of apical delivery is from an apical recycling compartment. The effect of PMA suggests that protein kinase C (PKC) is involved in the regulation of **pIgR** trafficking in MDCK cells. To test this the authors down regulated PKC activity by pre-treating cells with PMA for 16 h and obsd. that transcytosis could no longer be stimulated by PMA. Western blots show that the PKC isoenzymes .alpha. and to a lesser extent .epsilon., are depleted from MDCK cells which have been pre-treated with PMA for 16 h and that treatment of MDCK cells with PMA for 5 min causes a dramatic translocation of the PKC .alpha. isoenzyme and

a partial translocation of the .epsilon. isoenzyme from the cytosol to the membrane fraction of cell homogenates. This translocation suggests that the .alpha. and/or .epsilon. isoenzymes may be involved in PMA-mediated stimulation of transcytosis. A mutant **pIgR** in which serines 664 and 726, the major sites of phosphorylation, are replaced by alanine is stimulated to transcytose by PMA, suggesting that phosphorylation of **pIgR** at these sites is not required for the effect of PMA. These results suggest that PMA-mediated stimulation of **pIgR** transcytosis may involve the activation of PKC .alpha. and/or .epsilon., and that this stimulation occurs independently of the major phosphorylation sites on the **pIgR**. Finally, PMA stimulates transcytosis of basolaterally internalized transferrin, suggesting that PMA acts to generally stimulate delivery of endocytosed proteins to the apical surface.

L145 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:56667 HCAPLUS
DN 120:56667
TI New near-infrared cyanine dyes for labeling of proteins
AU **Lipowska, Malgorzata**; Patonay, Gabor; Strekowski, Lucjan
CS Dep. Chem., Georgia State Univ., Atlanta, GA, 30303, USA
SO Synthetic Communications (**1993**), **23**(**21**), **3087**-94
CODEN: SYNCAV; ISSN: 0039-7911
DT Journal
LA English
GI



I

AB Isothiocyanato-functionalized cyanine dyes I (X = O, S) for labeling of proteins at amino groups are synthesized. The dyes and their adducts with amines show strong absorbance and fluorescence in the near-IR region of 750-850 nm.

L145 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:1713 HCAPLUS
DN 120:1713
TI Gene transfer into respiratory epithelial cells by targeting the **polymeric immunoglobulin receptor**
AU **Ferkol, Thomas**; Kaetzel, Charlotte S.; Davis, Pamela B.
CS Dep. Pediatr., Rainbow Babies Child. Hosp., Cleveland, OH, 44106, USA
SO Journal of Clinical Investigation (**1993**), **92**(**5**), **2394**-400
CODEN: JCINAO; ISSN: 0021-9738
DT Journal
LA English
AB A system for targeting foreign DNA to epithelial cells in vitro has been developed by exploiting **receptor**-mediated endocytosis. The

polymeric Ig receptor transports dimeric IgA and IgM through epithelial cells, including those of the respiratory tract, by binding the **Igs** at the basolateral surface and transporting them across the cell. Fab fragments of antibodies directed against the extracellular portion of the **receptor**, secretory component, are similarly transported. Anti-human secretory component Fab fragments were covalently linked to a polycation, and complexed to various expression plasmids. When bound to an expression plasmid contg. the Escherichia coli lacZ gene ligated to the Rous sarcoma virus promoter, the complexes transfected HT29.74 human colon carcinoma cells induced to express **polymeric Ig receptor**, but not those lacking the **receptor**. Primary cultures of human tracheal epithelial cells grown on collagen gels, which induce the expression of **polymeric Ig receptor**, were also transfected with the complexes. From 5 to 66% of the respiratory epithelial cells had .beta.-galactosidase activity after treatment, comparable to the percentage of cultured human tracheal epithelial cells that express **polymeric Ig receptor** (8-35%). The addn. of excess human secretory component (Fab **ligand**) to the culture medium at the time of transfection blocked the delivery of DNA. The expression plasmid, either alone, complexed to the polycation, or complexed to a carrier based on an irrelevant Fab fragment, was not effective in transfecting either cell type. This DNA carrier system introduces DNA specifically into epithelial cells that contain **pIgR** in vitro.

L145 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:464318 HCAPLUS
DN 119:64318
TI Molecular cloning and exon-intron mapping of the gene encoding human transmembrane secretory component (the poly-Ig receptor)
AU **Krajci, Peter**; Kvale, Dag; Tasken, Kjetil; Brandtzaeg, Per
CS Lab. Immunohistochem., Norway
SO European Journal of Immunology (**1992**), **22**(9), **2309**-15
CODEN: EJIMAF; ISSN: 0014-2980
DT Journal
LA English
AB Secretory component (SC or the poly-**Ig receptor**) plays a crucial role in mucosal immunity by translocating **polymeric** IgA and IgM through secretory epithelial cells into external body fluids. Labeled restriction fragments from human SC cDNA were used to screen a human genomic leukocyte library. Three overlapping clones, spanning a total of 19 kb of the human SC gene, including 3 kb of the 5' flanking region, were characterized. The putative TATA box candidate, preceded by a CAAT-like box, was found 329 nucleotides upstream of the first exon. Altogether 11 exons covering the entire coding region were identified. The exon size ranged from 59 to 657 nucleotides and exon-intron junctions followed known consensus sequences. Three of the five extracellular **Ig**-related domains (D1, D4 and D5) were confined to one exon each (E3, E5 and E6), whereas D2 and D3 were encoded by the same exon (E4). The latter exon corresponds to that involved in alternate splicing of rabbit SC. The membrane-spanning segment was confined to part of one exon (E8). The cytoplasmic tail was encoded by four exons (E8-E11), whose boundaries encompassed fairly well the structural determinants proposed to be responsible for intracellular sorting of SC in the rabbit. The **polymorphic** restriction site reported earlier for PvuII was localized to the third intron.

L145 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1990:455160 HCAPLUS
DN 113:55160
TI Expression and analysis of the **polymeric immunoglobulin**

receptor in Madin-Darby canine kidney cells using retroviral vectors
AU **Breitfeld, Philip P.**; Casanova, James E.; Harris, Jeanne M.; Simister, Neil E.; **Mostov, Keith E.**
CS Med. Sch., Univ. Massachusetts, Worcester, MA, 01655, USA
SO Methods in Cell Biology (**1989**), **32**(Vesicular Transp., Pt. B), **329**-37
CODEN: MCBLAG; ISSN: 0091-679X
DT Journal; General Review
LA English
AB A review with 10 refs. describes method for studying the expression and transport of the **polymeric Ig receptor** (poly-IgR) in Madin-Darby canine kidney (MDCK) cells. Topic covered were expression of the Poly-IgR in MDCK cells, prodn. of **antibody** against rabbit secretory component, labeling of cells producing Poly-IgR and immunopptn., growth of cells on filters, pulse-chase anal. of cells on filters, and measurement of transcytosis.

L145 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1989:495175 HCAPLUS
DN 111:95175
TI Postendocytotic sorting of the **ligand** for the **polymeric immunoglobulin receptor** in Madin-Darby canine kidney cells
AU **Breitfeld, Philip P.**; Harris, Jeanne M.; **Mostov, Keith E.**
CS Whitehead Inst. Biomed. Res., Cambridge, MA, 02142, USA
SO Journal of Cell Biology (**1989**), **109**(2), **475**-86
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
AB The **polymeric Ig receptor** (pIg-R) is responsible for the **receptor**-mediated transcytosis of **polymeric Igs** (IgA and IgM) across various epithelia. The present study investigated the postendocytotic pathway of the **ligand** for the pIg-R. After a 5-min internalization at the basolateral surface, .apprx.45% of internalized **ligand** recycles to the basolateral medium and 30% is transcytosed to the apical medium. Why transcytosis of **ligand** is unidirectional, going only from basolateral to apical, but not from apical to basolateral, was also examd. Several factors could explain this, such as proteolytic cleavage of the pIg-R at the apical surface, decreased apical endocytosis of **ligand**, or an intracellular sorting event. The protease inhibitor, leupeptin, inhibits the cleavage of the pIg-R but does not alter the unidirectionality of transcytosis. In addn., there is a significant amt. of apical endocytosis of **ligand** (70% of that obsd. basolaterally). Apically endocytosed **ligand** can return only to the apical surface. Thus, once **ligand** reaches the apical surface, it is trapped and cannot return to the basolateral surface. It is proposed that unidirectionality of transcytosis is the result of intracellular sorting, and that this results from a signal(s) present on the pIg-R.

L145 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1988:184690 HCAPLUS
DN 108:184690
TI Novel antibody reagents: production and potential
AU **Williams, Gareth**
CS MRC Lab. Mol. Biol., Univ. Postgrad. Med. Sch., Cambridge, CB2 2QH, UK
SO Trends in Biotechnology (**1988**), **6**(2), **36**-42
CODEN: TRBIDM; ISSN: 0167-7799

DT Journal; General Review
LA English
AB A review with 40 refs. By use of genetic engineering and special hybridomas, monoclonal antibodies with dual specificities, predetd. specificities, or addnl. functional moieties can be produced.

L145 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1987:170223 HCAPLUS
DN 106:170223
TI Receptor-mediated in vitro gene transformation by a soluble DNA carrier system
AU **Wu, George Y.; Wu, Catherine H.**
CS Sch. Med., Univ. Connecticut, Farmington, CT, 06032, USA
SO Journal of Biological Chemistry (**1987**), **262**(10), **4429**-32
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB Foreign DNA can be specifically delivered to cells by a sol. carrier system that takes advantage of receptor-mediated endocytosis. The expts. were based on the following concepts: (1) hepatocytes possess a unique receptor that binds and internalizes galactose-terminal (asialo-)glycoproteins; (2) DNA can bind to polycations in a strong but noncovalent manner forming sol. complexes; and (3) the gene for chloramphenicol acetyltransferase, a bacterial enzyme that acetylates chloramphenicol, is not present in mammalian cells. Asialoorosomucoid (ASOR) was coupled to poly-L-lysine to form an asialoorosomucoid-poly-L-lysine conjugate. The plasmid, pSV2 CAT, was complexed to the conjugate in a molar ratio of 1:2. To test this complex, a model system was used consisting of hepatoma cell lines, Hep G2, asialoglycoprotein receptor (+), and SK-Hep 1, receptor (-). Each cell line was incubated with filtered ASOR.cntdot.poly-L-lysine.cntdot.DNA complex, or controls consisting of DNA plus ASOR, DNA plus poly-L-lysine, or DNA alone. Cells were assayed for the presence of chloramphenicol acetyltransferase activity as a measure of gene transformation. SK-Hep 1, receptor (-) cells, produced no detectable acetylated chloramphenicol derivs. under any condition. However, Hep G2, receptor (+) cells, incubated with the ASOR.cntdot.poly-L-lysine.cntdot.DNA complex were transformed as indicated by the presence of chloramphenicol acetyltransferase activity (0.028 chloramphenicol acetyltransferase units/106 cells). Mixts. of individual components of the complex failed to transform these cells. Competition by a 10-fold excess of ASOR prevented gene transformation by the ASOR.cntdot.poly-L-lysine.cntdot.DNA complex.

L145 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1986:127893 HCAPLUS
DN 104:127893
TI Distribution and processing of the **polymeric immunoglobulin receptor** in the rat hepatocyte: morphological and biochemical characterization of subcellular fractions
AU **Solari, Roberto**; Racine, Liliane; Tallichet, Corinne; Kraehenbuhl, Jean Pierre
CS Swiss Inst. Exp. Cancer Res., Epalinges, 1066, Switz.
SO Journal of Histochemistry and Cytochemistry (**1986**), **34** (1), **17**-23
CODEN: JHCYAS; ISSN: 0022-1554
DT Journal
LA English
AB Rat liver microsomes were fractionated and analyzed by immunochem. techniques for the IgA receptor (secretory component transmembrane form). The fraction enriched in the plasma membrane and rough endoplasmic reticulum contained predominantly a low-mol.-wt. form of the receptor [105 kilodaltons (kd)] which represents a core-glycosylated intermediate. In

the Golgi-enriched fraction, the receptor is present in its terminally glycosylated form and appears as a doublet with a mol. wt. of 115 kd. A lysosome-rich fraction contains both the 115 kd receptor and a 34 kd protein that was demonstrated by peptide mapping to be the membrane-anchoring domain of the receptor. Bile contains 31 kd and 29 kd proteins and hepatocyte cytosol contains a 32 kd protein that reacts with receptor-specific monoclonal antibody.

L145 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1985:94102 HCAPLUS
DN 102:94102
TI Antibodies recognizing different domains of the **polymeric immunoglobulin receptor**
AU **Solari, Roberto**; Kuehn, Lukas; Kraehenbuhl, Jean Pierre
CS Inst. Biochim., Univ. Lausanne, Epalinges, CH-1066, Switz.
SO Journal of Biological Chemistry (**1985**), **260**(2), **1141**-5
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The receptor responsible for the transepithelial transport of IgA dimer antibodies is a transmembrane glycoprotein known as membrane secretory component (SCm). During transport, the membrane anchoring domain is cleaved and the ectoplasmic domain of the receptor (SCs) remains tightly bound to the IgA dimer in exosecretions. Monoclonal antibodies were produced with distinct specificities against both cytoplasmic and ectoplasmic epitopes of rabbit liver SCm. One antibody (anti-SC303) reacted both with SCm and free SCs but not with SCs bound to IgA dimer (SIgA). Therefore, it recognized an epitope close to the IgA dimer binding site. The other monoclonal antibody (anti-SC166), which was unable to react with SCs, bound to the 15-kilodalton cytoplasmic extension of the membrane-spanning domain of the receptor. A polyclonal antibody (GaR-SC), raised in a goat against rabbit milk SCs, reacted with a subpopulation of SCs not recognized by the anti-SC303 monoclonal antibody and in addn. also reacted with covalently bound sIgA. The 3 antibodies cross-reacted with rat SCm. The ability of the anti-SC166 monoclonal antibody to immunoadsorb subcellular organelles as a result of the cytoplasmic orientation of its epitope thus is demonstrated. These data indicate that there are functional differences between the high- and low-mol.-wt. families of SC in terms of IgA dimer binding.

L145 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1985:94074 HCAPLUS
DN 102:94074
TI The primary structure of the human free secretory component and the arrangement of the disulfide bonds
AU **Eiffert, Helmut**; Quentin, Elmar; Decker, Joachim; Hillemeir, Sabine; Hufschmidt, Margarethe; Klingmueller, Dietrich; Weber, Michael H.; Hilschmann, Norbert
CS Abt. Immunchem., Max-Planck-Inst. Exp. Med., Goettingen, D-3400, Fed. Rep. Ger.
SO Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie (**1984**), **365**(12), **1489**-95
CODEN: HSZPAZ; ISSN: 0018-4888
DT Journal
LA German
AB The amino-acid sequence and the arrangement of the disulfide bonds of the free secretory component, isolated from colostrum from different women, were completely elucidated by the methods of protein chem. The free secretory component is a monomeric glycoprotein (mol. wt. .apprx.86,000), consisting of 558 amino acids with 7 carbohydrate chains bound to asparagine. The protein contains 20 cysteine residues but, as a special feature, no methionine. The polypeptide chain is divided into 5 regions

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                E MOSTOV K/AU
L2          121 S E3-E8
                E CHAPIN S/AU
L3           23 S E6,E10-E12
                E RICHMAN EISENSTAT J/AU
L4            8 S E3-E6
L5           18 S E21,E22,E30,E32
                E EISENSTAT/AU
                E LIGAND/CT
                E E38+ALL
L6        15394 S E1
L7       330572 S LIGAND
                E IMMUNOGLOBULIN RECEPTOR/CT
L8          185 S E89,E90
                E E4+ALL
L9         1556 S E10-E12
L10          62 S E85
L11         386 S E9 (L) POLYM?
                E PIGR
L12         206 S E3
L13        1316 S IMMUNOGLOB?(L)RECEPTOR(L)?POLYM?
L14         366 S L6,L7 AND L8-L13
                E IMMUNOGLOBULINS/CT
L15        6667 S E3 (L) FRAGMENT?
L16          25 S L14 AND L15
L17         366 S (L6 OR L7 OR ?LIGAND?) AND L8-L13
L18          25 S L15 AND L17
                E ANIMAL CELL/CT
L19       36281 S E3
                E ANIMAL ORGAN/CT
                E E3+ALL
                E E2+ALL
L20       30673 S E4,E5,E3
L21           9 S L17 AND L19
L22           1 S L17 AND L20
L23           9 S L21,L22
L24           6 S L18 AND L23
                E ANTIBOD/CT
                E E58+ALL
L25      154078 S ANTIBODIES/CT
L26         330 S L25 AND L8-L13
L27          44 S L26 AND L15
L28           5 S L27 AND L19,L20
L29           7 S L24,L28
L30          39 S L2-L5 AND (L6 OR L7 OR ?LIGAND? OR L25 OR ANTIBOD?)
L31          26 S L30 AND L8-L13
L32           3 S L30 AND L15
L33          27 S L31,L32
L34           2 S L33 AND L19,L20
L35           7 S L29,L34
L36          25 S L33 NOT L35
L37          36 S L2-L5 AND ?PIGR?
L38          49 S L33-L37
L39          12 S L30 NOT L38
L40          12 S L2 AND L3-L5
L41           2 S L3 AND L4,L5
L42          12 S L40,L41
L43           4 S L42 AND L38
L44          45 S L38 NOT L43
L45          39 S L44 AND (PD<=20000327 OR PRD<=20000327 OR AD<=20000327)
                SEL DN AN 23
L46           1 S E1-E3
L47           5 S L43,L46
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L48           5 S L35 NOT L47
L49         369 S ?PIGR?
L50        1490 S L8,L10,L11,L49,L13
L51         129 S L50 AND L25
L52          44 S L50 AND L15
L53           8 S L51,L52 AND L19,L20
L54           3 S L53 AND IMMUN?/SC
L55           2 S L54 AND LIGAND?/TI
L56           5 S L47,L55
L57          40 S L52 NOT L53-L56
                SEL DN AN 10 15
L58           2 S L57 AND E4-E9
L59           7 S L56,L58 AND L1-L58
L60           5 S L2-L5 AND P/DT
L61           3 S L60 NOT L59
L62           3 S L61 AND L1-L60
L63          10 S L59-L62
L64           6 S L63 AND ?SECRET?
L65           3 S L63 AND STALK?
L66          10 S L63-L65

     FILE 'HCAPLUS' ENTERED AT 07:05:26 ON 23 JUL 2003

     FILE 'BIOSIS' ENTERED AT 07:11:59 ON 23 JUL 2003
                E MOSTOV K/AU
L67         199 S E3-E7
                E CHAPIN S/AU
L68          33 S E3,E7,E9
                E RICHMAN /AU
L69          18 S E56,E60-E63
                E EISENSTAT/AU
L70         625 S ?PIGR?
L71        1132 S ?POLYM? (S) IMMUNOGLOB? (S) RECEPTOR
L72          72 S L67-L69 AND L70,L71
L73          70 S L72 NOT PATENT/DT
L74          66 S L73 AND PY<=2000
L75          25 S L74 AND 00520/CC
L76          24 S L74 AND CONFERENCE/DT
L77          25 S L75,L76
L78          41 S L74 NOT L77
                SEL DN AN 7 21
L79           2 S L78 AND E1-E4
L80           3 S L77 AND (?LIGAND? OR ANTIBOD?)
L81          22 S L77 NOT L80
L82          25 S L80,L81

     FILE 'BIOSIS' ENTERED AT 07:20:20 ON 23 JUL 2003

     FILE 'WPIX' ENTERED AT 07:20:45 ON 23 JUL 2003
L83          28 S L70/BIX
L84         140 S L71/BIX
L85           0 S ?POLYM? (S) IMMUNO GLOB? (S) RECEPTOR/BIX
L86         164 S L83,L84
L87          55 S L86 AND ?LIGAND?/BIX
L88         125 S L86 AND ANTIBOD?/BIX
L89          31 S L87,L88 AND SECRET?/BIX
L90          17 S L86 AND C07K016-28/IC,ICM,ICS,ICA,ICI
                SEL DN AN 5 16
L91           2 S L90 AND E5-E8
L92          19 S L86 AND C07K014-705/IC,ICM,ICS,ICA,ICI
L93          11 S L92 NOT L90
                SEL DN AN 8
L94           1 S L93 AND E9-E10
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L95          36 S L86 AND A61K039-395/IC,ICM,ICS,ICA,ICI
L96          20 S L95 NOT L90-L94
L97           3 S L91,L94
                E MOSTOV K/AU
L98           4 S E3,E4
                E CHAPIN S/AU
L99           2 S E3,E5
                E RICHMAN/AU
L100         43 S E3-E16,E20-E23
L101          4 S L86 AND L98-L100
L102          5 S L97,L101
L103          5 S L102 AND L83-L102
L104         28 S L89 NOT L103
L105         29 S L87 NOT L89-L104

     FILE 'WPIX' ENTERED AT 07:36:38 ON 23 JUL 2003
L106          1 S L102 NOT L101
                SEL PN L101

     FILE 'DPCI' ENTERED AT 07:39:30 ON 23 JUL 2003
L107          3 S E1-E19
                E MOSTOV/AU
L108          4 S E5,E6
                E CHAPIN S/AU
L109          1 S E5
                E RICHMAN E/AU
L110          3 S E3,E6
L111          5 S E9,E11
                E EISENSTAT/AU
L112          7 S L108-L111 NOT L107
L113          3 S L107 AND L108-L112

     FILE 'DPCI' ENTERED AT 07:41:21 ON 23 JUL 2003

     FILE 'HCAPLUS' ENTERED AT 07:49:01 ON 23 JUL 2003
L114          4 S US5972900/PN
L115          2 S WO9621012/PN
L116          1 S WO9746588/PN
L117          1 S ECKMAN ?/AU AND 1999/PY AND (21 AND 2 AND 246)/SO
L118          1 S KRAJCI ?/AU AND 1992/PY AND (22 AND 9 AND 2309)/SO
L119          1 S MOSTOV ?/AU AND 1994/PY AND (12 AND 63)/SO
L120          1 S FERKOL ?/AU AND 1993/PY AND (92 AND 5 AND 2394)/SO
L121          6 S (US5656469 OR US5658751 OR WO9600902)/PN
L122          1 S CARDONE ?/AU AND 1994/PY AND (124 AND 5 AND 717)/SO
L123          1 S LIPOWSKA ?/AU AND 1993/PY AND (23 AND 21 AND 3087)/SO
L124          2 S LEE ?/AU AND HETEROAROMAT? AND IMINIUM AND CYANIN? AND FLUORE
L125          1 S MAZANEC ?/AU AND 1995/PY AND (69 AND 2 AND 1339)/SO
L126          1 S WILLIAMS ?/AU AND 1988/PY AND (6 AND 2 AND 36)/SO
L127          1 S SOLARI ?/AU AND 1985/PY AND (260 AND 1141)/SO
L128          1 S EIFFERT ?/AU AND 1984/PY AND (365 AND 1489)/SO
L129          1 S SOLARI ?/AU AND 1986/PY AND (34 AND 1 AND 17)/SO
L130          1 S BREITFELD ?/AU AND 1989/PY AND (109 AND 475)/SO
L131          1 S PISKURICH ?/AU AND 1995/PY AND (154 AND 1735)/SO
L132          1 S FERKOL ?/AU AND 1995/PY AND (95 AND 493)/SO
L133          1 S WU ?/AU AND 1987/PY AND (262 AND 4429)/SO
L134          1 S BREITFELD ?/AU AND 1989/PY AND (32 AND 329)/SO
L135          1 S MOSTOV ?/AU AND 1994/PY AND (12 AND 63)/SO
L136          1 S MOSTOV ?/AU AND 1984/PY AND (308 AND 5954 AND 37)/SO
L137          1 S MOSTOV ?/AU AND 1980/PY AND (77 AND 12 AND 7257)/SO
L138          1 S WU ?/AU AND 1987/PY AND (262 AND 4429)/SO
L139          0 S HUDSON ?/AU AND 1980/PY AND 192/SO
L140          2 S (WO200047611 OR US6207195)/PN
L141         33 S L114-L140
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L142 31 S L141 NOT L66

FILE 'HCAPLUS' ENTERED AT 08:09:40 ON 23 JUL 2003
L143 26 S L142 AND L1-L66
L144 5 S L142 NOT L143
L145 31 S L143,L144